BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 23 1960

HIATUS HERNIA*

BY

N. R. BARRETT, M.Chir., F.R.C.S.

Surgeon, St. Thomas's Hospital and Brompton Hospital, London

Hiatus hernia is a common serious condition that affects the upper alimentary canal; and yet in 1940 nothing important was known about it.

Some surgeons, regarding it as a bizarre internal abdominal hernia, recognized the "paraoesophageal" variety, and cases of volvulus of the stomach had been described. Radiologists did not use the "head-down" position to test competence of the cardia, though Soresi (1919) had described this technique more than 20 years before. And endoscopists "peering through a glass darkly" (Allison, personal communication) had noted obscure inflammations and strictures that were "idiopathic." Morbid anatomists destroyed the evidence by eviscerating the parts and by cutting the oesophagus away from the stomach.

Thus, in spite of the intensive study of "indigestion" that occupied the physicians, and of countless laparotomies at which the appendix and the gall-bladder were hopefully removed, sliding hiatal hernia remained unknown and its complications arose without cause.

It was an Englishman, Philip Allison, who strung the isolated threads into one story. He defined hiatus hernia and pointed out how it differed from abdominal hernias in general, and from other diaphragmatic hernias in particular. His ideas, simple and correct, set research and treatment advancing upon the road of progress, and innumerable patients have benefited as a result.

In a number of papers published after 1940 Allison and many others have hammered the following things home.

Varieties of Hiatus Hernia

1. There are three principal varieties of hiatus hernia. These should be differentiated, not for anatomical reasons, but because they produce different pathological changes.

Paraoesophageal hernia, in which the cardia is normally placed, and the greater curve of the stomach together with the gastro-colic omentum herniates into a peritoneal sac in the mediastinum and through the oesophageal hiatus. This hernia scarcely concerns otolaryngologists, because the oesophagus is normal. It produces few symptoms in some cases, but may cause cardiac pain or arrhythmias, and the stomach in the mediastinum may develop a gastric ulcer or a carcinoma.

Sliding hiatal hernia is ten times more common than the paraoesophageal variety. It is a hernia *en glissade*, but the sac is unimportant because viscera from the abdomen do not get into it. This hernia, which occurs at all ages (Belsey (1952) reported one case in a child aged 3 weeks), matters for one reason only: it produces incompetence of the cardia, and this allows reflux of acid pepsin into the lower part of the oesophagus. It is a strange fact that the oesophagus should be vulnerable to the secretions of the stomach; but so it is. Reflux produces digestion of the gullet (oesophagitis), and this leads to a series of important pathological complications. The clinical story is typical—the principal symptoms being heartburn that occurs when the patient stoops or lies down, dysphagia of varying degrees, and symptoms that result from anaemia. The diagnosis of incompetence and sliding hernia is made radiologically, using the postural techniques that are now well known; and oesophagoscopy confirms the issue. There are many difficulties—mentioned below—associated with unravelling the causes of pain, anaemia, and dysphagia in these cases. The rational treatment is to make the cardia competent, and the simplest way of doing this is to reduce the hernia and fix the oesophago-gastric junction below the diaphragm.

"Mixed" or "rolling" hiatus hernias have features of both the above varieties.

2. Sliding hiatal hernia produces a short oesophagus, not vice versa. The sequence of events is hiatus hernia, reflux inflammation, spasm or fibrosis, shortening, stricture. "The term 'short oesophagus' is used to describe a condition in which the oesophago-gastric junction lies above the diaphragm and cannot be restored to its normal position below the diaphragm." (Ellis *et al.*, 1958).

3. Hiatus hernias are generally acquired, but may be congenital (see below): the term "congenital short oesophagus" is loosely and improperly used.

4. Gastric heterotopia and islands of ectopic gastric mucosa play no part in this story. These occur most commonly at the upper end of the gullet and are not known to be harmful.

In the remarks that follow I express my personal opinions and direct your attention entirely to matters that concern an otolaryngologist. What more should he know about hiatus hernia? How can he help in diagnosis? and, What are the limitations of endoscopic treatment? I shall assume that he will not be anxious to do a thoracotomy, or a laparotomy, except in critical circumstances.

Congenital Short Oesophagus

Before embarking on the subject of hiatus hernia the position as regards "congenital short oesophagus" must be clarified. This name is commonly and erroneously applied to sliding hiatal hernia in which the oesophagus is at first normal and a part of the stomach ultimately moves into the lower mediastinum. My own views about congenital short oesophagus have already been recorded (Barrett, 1956, 1958).

It would have been better if the term had never been introduced, because it has led to wrong thinking. I have never seen a patient in whom all the coats of the

*An Otolaryngology Lecture given at the Royal College of Surgeons of England on December 3, 1959.

oesophagus, normal in other respects, were congenitally short, and in whom a part of the stomach, as a consequence, lay in the mediastinum. Moreover, the fact that an infant is found to have a sliding hiatal hernia does not mean that the abnormality is congenital. But a condition exists to which the term congenital short oesophagus can legitimately be applied; though some consider that the anomaly is better described as the "lower oesophagus lined by columnar epithelium." In this we find that the gross anatomy of the gullet and of the stomach is normal to external and radiological appearances; and, in consequence, pathological changes that are detected are apt to be recorded as being "in the oesophagus." And here the question of nomenclature intervenes, for even among those who are well aware of the facts there are some who call the abnormal lower segment of the gullet "stomach" (as I was wont to do in times past) and others who refer to it as "oesophagus lined by columnar epithelium."

This confusion of terms matters because (1) the segment of the gullet lined by columnar epithelium is liable to the diseases that occur in the stomach, as opposed to oesophageal anomalies, and that is why some surgeons call it "stomach" in spite of its anatomy. (2) Allison has pointed out, and I confirm, that in a proportion of cases in which the lower oesophagus is lined by columnar epithelium there is, in addition, a sliding hiatal hernia. Such a patient has, from above downwards, oesophagus lined by squamous epithelium, oesophagus lined by columnar epithelium, and then a sliding hiatal hernia above the diaphragm.

The explanation of how such a deformity occurs is not understood; but let us be clear that it has nothing to do with "islets of ectopic gastric mucosa." In my view it represents a failure in the developmental evolution of the foregut that occurs when the embryo is between 3 and 100 mm. in length (Johns, 1952). This area is at first lined by columnar epithelium that proliferates exceedingly until ultimately the lumen becomes obliterated. After a short time the channel is re-established by the formation of numerous clefts that fuse into one pathway. It is only at the conclusion of these complicated metamorphoses that the oesophagus acquires its "normal" squamous epithelium. I believe that when the lower oesophagus is lined by columnar epithelium this cycle may not have been completed.

A surgeon using an oesophagoscope for diagnostic purposes must be aware of this developmental fault, because the treatment of the diseases that are associated with it differs from that appropriate to sliding hiatal hernia. There is, for instance, no question of replacing the segment lined by columnar epithelium below the diaphragm; it has always been in the mediastinum, and it is anchored there by its segmental aortic blood-supply.

A lower oesophagus lined by columnar epithelium may cause oesophagitis and its complications, and it is the usual source of columnar-cell carcinoma that originates in the gullet as opposed to the stomach. In the lower segment typical gastric ulcer occurs.

Diagnosis

With these facts in mind it would be nice to be able to tell you that diagnosis of these cases is easy. Unfortunately this is not the case; but there are pointers that may help.

1. The majority of sliding hiatal hernias (from which this condition must be distinguished) are small; in them the hernia seldom extends upwards more than 5 cm. above the hiatus. If the change from squamous to columnar epithelium occurs higher than this in the mediastinum—a point that can be suggested radiologically but can be verified at endoscopy—the condition should be suspected.

2. If there is doubt the surgeon should put one or more silver clips (such as are used by the neurosurgeons to secure haemostasis) upon the point of transition of the mucosa. Special forceps are available that enable this to be done through an oesophagoscope. These clips can then be seen in radiographs and their position relative to the apparent oesophago-gastric junction (the cardia) noted.

3. When a biopsy specimen is taken from the oesophagus at endoscopy, an attempt should be made to get a piece of the mucous membrane below the lesion. In the case of simple sliding hiatus hernia the fact that this mucosa proves to be gastric does not come as a surprise; but if the lesion under investigation happens to be situated in the middle or the upper part of the gullet, and if, in addition, the gut below it has the typical radiological appearances of "oesophagus," the information should transform the picture of diagnosis and treatment.

Sliding Hiatal Hernia

Aetiology and Pathology of Oesophagitis

Since the pathology and the treatment of most hiatal hernias hinges upon the failure of the barrier to reflux that should exist between the stomach and the gullet, you must be familiar with some aspects of this subject.

Wangensteen and Leven (1949) and Ferguson *et al.* (1950) have shown that all the changes we now recognize as "oesophagitis" can be produced by perfusing the lower part of the gullet with acid-pepsin. Within a few hours the mucosa is destroyed, and eventually perforation occurs. In man the process is less drastic because the insult is not continuous. They also showed that hydrochloric acid alone, in physiological strengths, is not harmful, but that the secretions normally present in the duodenum are dangerous. Anybody who has treated a patient with a duodenal fistula knows the damaging effects upon the skin of the abdominal wall and can visualize what goes on in the oesophagus.

In 1953 Aylwin did experiments that showed how the gullet of a normal individual is protected by day against the ravages of reflux. Not only is the cardia competent, but the lower oesophagus is coated with mucus and bathed by alkaline saliva. When a patient who has a sliding hiatus hernia stoops down or lies flat at night, these defences become inefficient. The most damaging secretions may come from the mucous membrane of the pouch that lies above the diaphragm, and not from the main part of the stomach in the abdomen.

The histological changes that occur in the lower oesophagus have been studied at operations by surgeons and in necropsy specimens by Peters (1958). The salient features of oesophagitis are:

It affects the oesophageal mucosa alone at first, and is sharply limited by the gastric mucosa below. It is most pronounced at the point where the epithelium changes from squamous to columnar. One reason that recognition of "oesophagitis," as a real entity, was so long delayed was that the red, angry surface that the endoscopist sees fades completely as soon as the tissues are removed from the body, and there may be little to see at necropsy.

The microscopical changes exceed those seen with the naked eye.

The pathology is of inflammation. There are elements of acute and chronic type, implying repeated clinical episodes.

Each layer of the oesophageal wall protects for some time the one external to it, so that after an acute exacerbation there is a terraced destruction.

Shallow epithelial ulcers occur and may heal completely or lead to leucoplakia.

After the submucosa has been destroyed the lesion generally progresses through the muscle coats, producing, not a penetrating ulcer, but a tumorous mass of inflammatory tissue that becomes fixed in the mediastinum by perioesophageal adhesions and adenitis.

Inflammatory oedema, congestion and thrombosis of blood vessels, fibrosis, and scar play their parts.

The time taken for these changes to occur varies within wide limits, and the reasons for this are obscure.

Barrier Against Reflux

This subject has become confused because two different types of information have been overlaid.

On the one hand, physiologists, studying the mechanisms of swallowing and vomiting, have worked out certain pressure barriers, pressure changes, flap valves, and mucosal rosettes that exist and operate in normal subjects.

On the other hand, surgeons know that when a patient has a sliding hiatal hernia reflux occurs spontaneously into the lower oesophagus. Moreover, they know that reflux is immediately controlled by replacing the oesophago-gastric junction in the abdomen. They infer that competence of the cardia depends upon physical conditions (such as the difference in pressures in the lower mediastinum and in the abdomen, in the angle at which the gullet joints the stomach, and in the pressure of a length of oesophagus below the hiatus) rather than upon physiological sphincters, pinchcock effects of the diaphragm, or aberrations of nerve supply to the cardia. The idea that the hiatus is a pinchcock dies hard with otolaryngological surgeons; the time has come when they must accept that this hiatus in the diaphragm is not a sphincter, but simply the point at which the pressure upon the gullet changes from relatively negative to positive.

Relation Between Symptoms of Oesophagitis and Presence of a Sliding Hernia

The importance of oesophagitis as a cause of a special kind of dyspepsia has been proved beyond dispute. But, whereas in the past this explanation was not known, it is possible that nowadays too much blame is laid at this particular door. In my experience it is common for bleeding into the bowel of unknown cause to be attributed, without sufficient reason, to oesophagitis.

Peters (1958) says that 29% of the cases he examined at necropsy had lesions such as gastric ulcer, duodenal ulcer, or cholecystitis, as well as oesophagitis. This statement underlines the necessity for making sure not only that an individual patient has a hiatus hernia but that the symptoms of which he complains are due to this condition.

It is certain that not all those who have a hiatus hernia are ill, though they stand in danger of becoming so. Occasionally heartburn occurs in normal individuals, and we must remember that the cardia becomes physiologically incompetent whenever we vomit. Some people who have symptoms such as heartburn have no demonstrable hernia; others have reflux that can be demonstrated radiologically and complain of nothing relative to the oesophagus. The size of a hernia that a radiologist sees bears no relation to the severity of the pathological changes or to the symptoms it can produce. Small damaging hernias require treatment as urgently as those that are larger.

There is a small but important group of patients whose oesophago-gastric junction is apparently below the diaphragm and competent, but who have oesophagitis. These are the cases in which the lower oesophagus is lined by gastric epithelium (congenital short oesophagus). And yet another group, emphasized by Lortat Jacobs, of Paris, have no abdominal oesophagus, and therefore have reflux without obvious cause. Creamer *et al.*, (1959) at St. Thomas's, have shown the importance of having a length of the oesophagus that is subjected to positive abdominal pressure below the diaphragm.

Reflux oesophagitis waxes and wanes, and there are patients whose symptoms are of long duration who have limited destruction in the gullet. On the other hand, oesophagitis that has permeated and invaded the full thickness of the gullet can occur in a few weeks or months; and one of the outstanding problems at the moment is to assess the severity and the permanence of the damage before embarking upon treatment that can be difficult and dangerous.

Endoscopic Appearances

The endoscopic appearance of oesophagitis are well known; but even experienced operators may be uncertain of what they see upon occasion. Hence the necessity for biopsy in all cases.

An important reason for this difficulty in interpretation is that in acute inflammation there will certainly be some bleeding beyond the point of the oesophagoscope, and this obscures the view. This condition bleeds more easily than does a malignant growth, but oesophagitis and a neoplasm may coexist. A normal oesophagus should be empty. Retained secretions or food suggest a hold-up at or above the cardia. The reaction of the oesophageal contents should be tested with Congo red paper: an acid reaction suggests reflux. An incompetent cardia is patulous and easily passed with the tip of the oesophagoscope (the instrument must be long enough to enter the stomach) and drops of gastric juice can often be seen welling back as the patient breathes. But all these things may be wanting and oesophagoscopy may be negative in a patient who yet needs surgical treatment: therefore, do not be dogmatic in your report. It is a serious mistake to miss a carcinoma of the stomach or of the lower part of the oesophagus. A malignant growth near the cardia can cause incompetence and reflux, leading to oesophagitis above it. Growths in this position are notoriously difficult to show radiologically. For this reason it is wise to get a biopsy not only of the inflamed oesophagus but blindly of the stomach beyond. Where doubt persists laparotomy is mandatory.

A hiatus hernia that is causing symptoms is generally suspected clinically, diagnosed radiologically, and confirmed at thoracotomy. The importance of endoscopy is to get extra evidence, to assess the extent and position of lesions such as oesophagitis, and to eliminate malignant disease.

In the case of paraoesophageal hernia the endoscopist confirms that the cardia is below the diaphragm, and that it is competent. The former can be done only in a patient who is breathing naturally, because it depends upon noting the absence of respiratory oesophageal hiatus. The oesophagus itself is normal in these cases.

Ulceration

Apart from carcinoma, there are several distinct types of ulceration that occur in these cases. The first is ulceration situated in the squamous epithelium of the oesophagus itself above the oesophago-gastric junction. These ulcers are generally small, discrete, and shallow; they tend to heal; they cannot be shown radiologically; and they never perforate.

When the ravages of penetrating oesophagitis have transgressed the coats of the gullet and formed a mass of contracted muscle and scar (see below) the epithelium that lined the affected area disappears for most of the length of the stricture, and the lumen that remains is ulcerated—granulating, septic, and tortuous. The lesion that results is a stricture that may be short or long; but at oesophagoscopy one gets an entirely false impression of what has happened because only the entrance to the lesion can be seen, and the mucosa in the vicinity is often remarkably normal. Nor is it possible to assess the length or the penetration of the pathological process at oesophagoscopy.

Ulcers that occur in the pouch of stomach that forms a sliding hiatal hernia are true gastric ulcers (Barrett, 1950) and have nothing to do with reflux. They were originally described by Rokitanski, though he did not understand their aetiology. They are difficult to see at oesophagoscopy because there is often oesophagitis or a stricture at the oesophago-gastric junction above the ulcer. Allison and Johnstone (1953) described the radiological appearances. Many such ulcers are diagnosed for the first time at operation, and sometimes they cause massive or fatal bleeding by penetrating the heart or the aorta.

Gastric ulcers and carcinoma also occur in the stomachs of those with paraoesophageal hernias, but these are beyond diagnosis endoscopically.

Bleeding and Anaemia

At a conservative estimate 10% of patients who have oesophagitis have anaemia severe enough to affect the symptoms. Considering how easily the inflamed mucosa bleeds at oesophagoscopy, it is surprising that massive haematemesis and melaena are uncommon. The fact is that occult blood in the stools is often difficult to detect, even when the haemoglobin has been severely reduced; this is probably because the bleeding is intermittent. Haematemesis is rare. The anaemia that occurs in these cases is hyperchromic and microcytic; it responds to cure of the oesophagitis and to the administration of iron.

It is a mistake to attribute anaemia of unknown intestinal origin to oesophagitis unless there is an obvious inflammation in the lower oesophagus, and unless all the usual causes have been systematically eliminated.

It is useless and meddlesome to treat bleeding, caused by oesophagitis, by local applications of caustics or styptics.

Stricture of the Oesophagus

Stricture is at once the most crippling and the most dangerous complication of oesophagitis: crippling because the patient ultimately starves; dangerous because treatment can only alleviate, and that at a risk. It is my opinion that even when a stricture has been wisely and successfully treated the patient will never be quite normal again. The normal oesophagus is irreplaceable.

Apart from malignant disease and the effects of swallowed corrosives, oesophageal strictures are, in practice, due to reflux. Congenital, idiopathic, and specific strictures are so rare as to be suspect. Do not make these diagnoses, and do not act on them, unless you are sure of your ground.

When a patient complains of dysphagia and a radiologist reports incompetence of the cardia and a hiatus hernia, and when, in addition, there is a stricture in the lower 2 to 3 in. (5 to 7.5 cm.) of the mediastinum, one can assume that the gullet below the stricture is lined by columnar epithelium whatever its external shape or radiological appearance. But if the stricture is due to carcinoma or to a swallowed corrosive the epithelium will be squamous, above and below the stricture. This fact is important.

A stricture that is causing dysphagia is nature's way of protecting the lower oesophagus against further episodes of digestion. This truth was first impressed upon my mind in the following circumstances.

A child was admitted to Horton War Hospital suffering from dysphagia since birth. A barium-swallow examination showed a long, narrow stricture in the lower part of the gullet. At that time neither the pathology of these lesions nor their treatment was clear. At oesophagoscopy the lower oesophagus contained residue, and the entrance to the stricture was of pinhole size. But the mucous membrane above the stricture was normal; there was no ulceration or inflammation. The stricture was dilated with appropriate skill, and the immediate result was that the child "could swallow anything." A few days later, with the design of completing the good work, another oesophagoscopy was done, and the appearance of the mucosa above the stricture was dramatically changed. It was fiery red and haemorrhagic.

The third thing about a stricture due to reflux is that neither the clinical story nor the radiological appearances nor the findings at oesophagoscopy enables us to be certain of the precise extent of the lesion. There are a variety of strictures associated with oesophagitis, and they may be combined or separate.

The radiological appearances of stricture can be produced by muscle spasm. This happens in most cases of acute oesophagitis, and is especially deceptive when there is a small carcinoma high on the lesser curve of the stomach. It has been said that spasm may follow vagotomy; but I doubt this, and believe that the explanation of the recorded cases is that the dysphagia was secondary to the trauma of the operation.

Spasm due to the irritation of oesophagitis may be complicated by vascular congestion and oedema, and these can reduce the lumen of the gullet to a chink, and cause serious dysphagia.

"Strictures" due to oedema or vascular congestion vary in intensity and are not permanent. As the acute episode of oesophagitis wanes they disappear and the patient may swallow again. But when the destructive changes that follow repeated episodes of oesophagitis extend through the submucosa and the muscles, the

lesion becomes permanent. And the fact that this final phase has been reached can be verified only at operation, though it will have been suggested by the story, the *x*-ray films, and oesophagoscopy.

The steps by which the gullet is destroyed have been studied at St. Thomas's Hospital by making histological sections of every stricture we have excised; certain problems have been revealed (Barrett, 1958). There has been a tendency to assume that fibrosis and scar accounts for all that occurs; but this is not so. Nor can it be assumed that an oesophageal stricture is comparable to a gastric ulcer or an hour-glass stomach. Here are the facts.

After repeated episodes of oesophagitis in some patients, and soon after the first clinical trouble in others, fibrous tissue begins to accumulate in the submucosa. It is vascular, young, cellular, and oedematous at first. It may have intact squamous epithelium upon its surface, and it produces a palpable hard lump that generally surrounds the gullet. So hard may this tumour be that carcinoma may be confidently diagnosed in error.

In a few cases the process stops at this stage: the oedema settles, and a ring of fibrous tissue in the submucosa is the result. A stricture of this type is usually sited where the mucous membrane changes; but it may be lower down, and, in this event, it has columnar epithelium above it.

"Oesophagitis" is a progressive disease in most cases, and sooner or later the inflammation invades the muscle coats of the gullet. When this has happened sections show a fibromuscular lump about the size of a chestnut. Both the muscle layers are strikingly thicker than normal and the submucosa is completely replaced by scar. The mucosa may or may not be deficient, and the lumen is greatly narrowed throughout the length of the lesion. Swallowing is seriously obstructed.

At this stage the lesion is different from a peptic ulcer in the stomach or the duodenum. It is not an ulcer but a mass of tissue that feels very hard. The fibroblasts do not destroy the muscle, but grow in strands between the bundles. When the inflammatory reaction has reached the mediastinum most of the original muscle is still extant, though the nuclei are abnormal in places and some of the vessels are thrombosed.

We believe that the accretion of muscle that forms so much of the bulk of these strictures is due to a concertina effect. As the scar in the submucosa contracts it heaps the muscle bundles together on its outer surface, thus adding to the bulk of the tumour and the severity of the dysphagia.

Once the inflammation reaches the outer side of the gullet the tissue planes in the mediastinum become oedematous and the adjacent lymph nodes enlarge. The strictured area is now adherent to the pericardium anteriorly, to the aorta at the back, and to the pleura and pulmonary ligaments laterally. There is one other factor that is relevant. As the blood-vessels in the submucosa are replaced by scar, the life of the muscle depends upon vessels that enter from the surface and run towards the lumen. In advanced cases recovery becomes impossible because these vessels thrombose, the muscle atrophies, and nothing but scar remains.

Treatment

Considering the histological changes, one may venture an opinion on treatment. Once a fibrous stricture has begun to form, medical treatment is unlikely to relieve dysphagia. Two things must now be done: (1) prevent any further reflux of acid-pepsin, and (2) re-establish the lumen of the gullet. Neither alone yields more than passing benefit; and simply to dilate a stricture of this kind is like blowing up a tyre that has a puncture.

When the clinical history is short and dysphagia not serious, when the narrowing is not gross, and when repeated barium-swallow examinations show variations in the outline and size of the narrow segment, one may hope that congestion, spasm, and oedema will subside after surgical reduction of the hiatus hernia. If the patient happens to have a lower oesophagus lined by columnar epithelium (as opposed to a hiatus hernia) surgical reduction is not feasible, and more drastic measures are necessary.

If reflux has been controlled, and an annular stricture remains in the submucosa, some say that the lumen can be most effectively re-established by excising the scar. This has been done by exposing the mass at thoracotomy, incising the muscle coats down to the scar in the line of the bowel, and cutting out the ring of scar. The mucosa in these circumstances regenerates quickly. The merits of this procedure, as opposed to repeated dilatations from within, are matters for individual decision. So, too, are plastic operations to enlarge the lumen.

But if the scar has penetrated through and beyond the muscle and fixed the tumour in the mediastinum, nothing short of excision of the abnormal segment gives a permanent result. After excision the question of how to bridge the gap looms large, and is debatable. My own preference, at the moment, is to transpose an isolated loop of small bowel or colon, and to place this between the proximal part of the oesophagus and the stomach.

It is fair to underline these points: that, before operation, nobody as yet knows how to diagnose the extent and permanence of the destructive changes in the gullet; that the possible benefits of corticosteroids at certain phases in the disease are under debate; and that, once a permanent stricture has formed, the best operation to perform remains a matter of personal opinion.

In the past there has been a tendency to dodge these issues, chiefly because exacting surgical procedures are necessary, and to devise less difficult operations. This would be praiseworthy if the rationale of the new procedures did not defy existing knowledge.

The problems involved in treating stricture of the oesophagus due to oesophagitis are technically more involved than those that occur in the management of carcinoma. Do not embark upon resections without thought; and learn from the mistakes of those who have travelled the road.

Conclusions

I recall some advice that William Mayo, that wise man of surgery, gave me 25 years ago. "Do not," he said, "attempt an important lecture unless you have at least one thing to say." Here, then, is the message that I hope you will think about and accept:

Do not dilate strictures due to oesophagitis unless you can effectively and permanently prevent reflux of acid-pepsin at the same time. In infants, and in old people, it may be justifiable to temporize upon occasion; but the issue is clear in most cases.

"Why not dilate strictures?" you ask. "The operation is safe in competent hands; the immediate results are gratifying; the risks of alternative operations are considerable; and histological preparations have shown that, even in patients who have had a long clinical history of dysphagia, muscle may predominate over scar in the 'tumour.' Moreover, many patients have been jockeyed along from year to year by repeated endoscopies."

The case against dilatation is this. Immediate relief of dysphagia is no criterion of cure. By stretching a stricture of this sort nature's barrier against reflux is broken down, and the inexorable complications of oesophagitis are rekindled to flame again. With each exacerbation the scar, that remains for ever, penetrates the muscle of the gullet more deeply and rises upwards in the mediastinum. The end is worse than the beginning.

BIBLIOGRAPHY

Allison, P. R. (1946). *J. thorac. Surg.*, **15**, 308.
—— (1948). *Thorax*, **3**, 20.
—— (1951). *Surg. Gynec. Obstet.*, **92**, 419.
—— and Johnstone, A. S. (1953). *Thorax*, **8**, 87.
—— —— and Royce, G. B. (1943). *J. thorac. Surg.*, **12**, 432.
Aylwin, J. A. (1953). *Thorax*, **8**, 38.
Barrett, N. R. (1950). *Brit. J. Surg.*, **38**, 175.
—— (1954). Ibid., **42**, 231.
—— (1956). Communication to 5th meeting of L'Association des Sociétés Européennes et Méditerranéennes de Gastro-Entérologie. London.
—— (1958). In *Modern Trends in Gastro-enterology*, edited by F. Avery Jones, 2nd ser., p. 147. Butterworth, London.
—— Franklin, R. H. (1949). *Brit. J. Surg.*, **37**, 194.
Belsey, R. (1952). In *Modern Trends in Gastro-enterology*, edited by F. Avery Jones, 1st ser., p. 128. Butterworth, London.
Collis, J. Leigh, Kelly T. D., and Wiley, A. M. (1954). *Thorax*, **9**, 175.
—— (1957). Ibid., **12**, 181.
Creamer, B., Harrison, G. K., and Pierce, J. W. (1959). Ibid., **14**, 132.
Ellis, F. H. (1959). *Surg. Gynec. Obstet.*, **109**, 101.
—— Andersen, H. A., Clagett, O. T. (1958). *Ann. Surg.*, **148**, 526.
Ferguson, D. J., Sanchez-Palomera, E., Sako, Y., Clatworthy, H. W., Toon, R. W., and Wangensteen, O. H. (1950). *Surgery*, **28**, 1022.
Johns, B. A. E. (1952). *J. Anat. Lond.*, **86**, 431.
Johnstone, A. S. (1954). *Radiology*, **62**, 750.
Kelly, A. B. (1939). *J. Laryng.*, **54**, 621.
MacLean, L. D., and Wangensteen, O. H. (1956). *Surg. Gynec. Obstet.*, **103**, 5.
Moersch, R. N., Ellis, F. H., McDonald, J. R. (1959). Ibid., **108**, 476.
Peters, P. M. (1955). *Thorax*, **10**, 269.
—— (1958). Ibid., **13**, 1.
Smithers, D. W. (1957). *Ann. roy. Coll. Surg. Engl.*, **20**, 36.
—— (1956). *Thorax*, **11**, 257.
Soresi, A. L. (1919). *Ann. Surg.*, **69**, 254.
Stewart, M. J., and Hartfall, S. J. (1929). *J. Path. Bact.*, **32**, 9.
Wangensteen, O. H., and Leven, N. L. (1949). *Surg. Gynec. Obstet.*, **88**, 560.

The number of emergency calls received by the London Ambulance Service continues to increase. In a report to the Health Committee Dr. J. A. SCOTT, the medical officer of health, says that 104,983 calls were received in 1959; in 1958 the number was 99,188 and in 1957 97,535. Calls to street accidents in 1959 numbered 21,701, 2,519 more than the previous year. Despite the extra journeys the average time taken by ambulances to reach the scene of accidents was only a fraction of a minute longer than 1958—6.6 minutes instead of 6.5. On average, patients were admitted to hospital 20.9 minutes after the calls for help were received. There were the usual peak hours for the different kinds of call—maternity cases between 3 and 4 o'clock in the morning, home accidents at midday, street accidents in the late afternoon and early evening, and cases of assault towards midnight. Maternity cases, however (27,429 of them), continued to outnumber all others.

ON VIRUS METABOLISM AND NEOPLASIA

BY

DAVID S. NELSON, M.B., B.S.

AND

P. M. de BURGH, M.B., B.S.

Department of Bacteriology, University of Sydney, Australia

The term "virus" covers a range of organisms varying widely in physical and biological properties. One common feature is that all are obligate intracellular parasites. No valid evidence has been produced that any virus—bacterial, plant, or animal—possesses any equipment which would allow it metabolic activity in its own right, and it is generally assumed that virus multiplication is dependent on the metabolism of the host cell. The study of "virus metabolism" therefore resolves itself into the search for modifications of the metabolism of the host cell in the course of viral infections. With phage-infected bacteria this has been most profitable, but with infected animal tissues has so far only scantly illuminated the problem of virus multiplication.

Several limitations must be imposed on the interpretation of biochemical changes in virus-infected tissues. When only a small proportion of cells in the tissue are infected compensatory changes may occur in adjoining cells, so that a composite picture is presented of cells under the influence of two stimuli. This applies not only to complex tissues *in vivo* but also to tissue cultures containing only one cell type. The effects of infiltration with inflammatory cells can usually be excluded, either by adequate histological control or by the nature of the host tissue—that is, in tissue culture. Alterations in the overall metabolic activity of a tissue may occur owing to necrosis of some cells. It is important not to confuse the changes secondary to cell death with those causing cell death. For this reason, studies on tissues late in the course of viral infection (and damage) must be interpreted with great reserve. In general, the earlier a change is observed the more likely is it to be primarily induced by the virus.

Substances other than virus contained in the inoculus may also produce metabolic alterations, and this possibility must be excluded by inoculation of controls with material of similar origin not containing virus. Finally, where single enzyme activities are measured, alterations may be due not only to an absolute increase or decrease in the quantity or activity of apoenzyme or coenzyme, but also to a "diluted" or "concentration" effect of an increase or decrease in the amount of fat or water in the individual cell, or the amount of extracellular fluid in the tissue. Estimation of water and lipid in the tissue and calculations of activities per unit dry or lipid-free dry weight deals satisfactorily with this potential course of error.

Ectromelia virus multiplying in mouse liver forms a virus-host system for which these objections and limitations are not serious.

The activities of various enzymes in this system have been estimated and in part reported (de Burgh, 1957; Nelson and de Burgh, 1958, 1959). These have been compared with similar estimations in regenerating mouse liver. In this case new normal liver is rapidly reproduced and cell division occurs; this may be taken

as an example of normal or balanced growth. The cytoplasm of ectromelia-infected liver increases in the absence of cell division, while in neoplastic liver cell division predominated over cytoplasmic growth. Both are in effect examples of different types of unbalanced growth. The fact that growth is "unbalanced," rather than any similarity in the type of imbalance, has prompted this discussion.

Though the virus theory of neoplasia may not be valid as a general proposition there is considerable interest in the idea that both the virus-infected cell and the cancer cell are subject to a disorder in the "replication of specific pattern" (Burnet, 1956). The neoplastic change ultimately induced by chemical carcinogens is thought to be due possibly to the gain and subsequent loss of an antigenic marker (Green, 1954), while the virus-infected cell may suffer damage directly or indirectly as a result of the production of "foreign" nucleic acids and protein. Disordered growth and macromolecular change seem to be associated. In each case metabolic alterations accompany these changes. It seems profitable to compare our observations on ectromelia-virus-infected and regenerating livers with those made by others on spontaneous, induced, and transplanted liver tumours of mice and rats; on the livers of mice and rats carrying tumours at other sites; and on the changes induced by viruses multiplying in other tissues, so far as these can be interpreted. It has been suggested (Bauer, 1953) that the diversion of basic precursors (amino-acids, purines, pyrimidines, etc.) may be the cause of alterations in enzyme activities in virus-infected tissues. Therefore the comparison includes enzyme changes occurring in nutritional deficiencies. Finally, foetal liver is included, as neoplastic tissue is sometimes said to be metabolically more primitive than its parent tissue.

It is apparent even from this limited survey that there is no consistent pattern of enzyme changes in virus-infected tissues or in various hepatic neoplasms. In neither case has any completely characteristic biochemical change yet been described. The lack of specificity suggests the possibility that some changes might be quite incidental to the process of virus multiplication or neoplasia.

The remainder of this discussion is concerned with the following three factors. (*a*) *A possible mechanism of production of these changes in virus-infected cells, based on competition between nucleic acids of virus and host cell.*—It is suggested that metabolic changes occur partly as a result of inhibitions of replication or turnover of a host component for the synthesis of which a particular type of nucleic acid (N.A.) is the template, and partly as a compensation by the host cell for these changes. It is not thought necessary for these changes to be purposeful.

(*b*) *The applications of such a mechanism in explaining the host specificity of viruses and the occurrence or otherwise of a cytopathic effect.*—Host specificity could be explained on the basis of structural similarity between virus and host cell N.A. Cytopathogenicity may be determined by the inhibition of particular N.A. templates by a virus N.A. leading to disturbance of a key metabolic pathway or to loss of an essential structural component of the cell.

(*c*) *The relation between the virus-induced metabolic changes and carcinogenesis.*—Virus infection can produce changes in cells which are analogous to those which appear to occur in neoplastic cells—namely, metabolic change and unbalanced growth. The possible role in carcinogenesis of a process similar to the competition between N.A.s suggested for virus infection is discussed.

Virus Metabolism and Virus Multiplication

When a cell is infected by a virus the virus appears to break partly or wholly into non-infectious particles which are thought to be the actual multiplying units. The fact that purified (protein-free) N.A. from some viruses is infective suggests that these units are N.A. and that virus-specific protein is not essential to multiplication. Some form of competition between virus and host N.A. must occur (Gottschalk, 1957). They may compete for either N.A. or protein precursors or for the energy to incorporate these precursors. The success of the virus components may be due to lowered entropy. When the virus components succeed there are two results (Fig. 1).

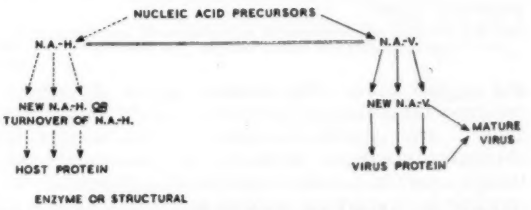


FIG. 1.—N.A.-H.: Host nucleic acid (R.N.A. or D.N.A.). N.A.-V.: Virus nucleic acid (R.N.A. or D.N.A.). ═══: Competition. - - - -: Inhibition.

1. *Replication of virus components, usually followed by the appearance of new infectious virus.*—In ectromelia-infected mouse liver this is reflected in a 10^2–10^6-fold increase over the original titre.

2. *Inhibition of the replication or turnover of the host component.*—On current views of protein synthesis this would be reflected in a decreased synthesis of the specific protein of which that N.A. unit (or its derivative) was the template. This would occur whether the competition were for N.A. or for protein precursors. Decreased activities of some enzymes would be one reflection of this. There seems to be no need to ascribe purpose to the decreases in some enzyme activities, as they could occur as a result of a chance similarity between virus and host template. The effects on cell metabolism of purified N.A. from viruses (or other sources) and the association of different metabolic changes with different fractions of nucleic acids from the same source would obviously be of interest.

Any hypothesis of the metabolic effects of virus multiplication must also explain why there are increases in certain enzyme activities. On the hypothesis outlined above it is necessary to consider these as a compensatory response to the inhibition of some metabolic pathways as a result of virus infection. This involves the concept of a feed-back mechanism. This could conceivably occur at any of three levels (Fig. 2). (1) In the case of a rapidly turning-over enzyme, inhibition of its synthesis would soon result in a decrease in its level of activity and an accumulation of one or more metabolites. This accumulation could be the stimulus to increased production of the enzyme(s) of an alternative pathway. The metabolite might be an intermediate in the synthesis or breakdown of any cell component including coenzymes. (2) The decrease in enzyme 1 might be the information according to which enzyme 2 is produced in increasing

amounts. (3) The decrease in N.A.$_1$ may directly or indirectly stimulate the synthesis or turnover of N.A.$_2$ - Xanthine dehydrogenase activity of mouse liver is found to be increased very early in the course of ectromelia-virus infection, before the appearance of either new virus or complement-fixing antigen (Nelson and de Burgh, 1959). If, as appears likely, this is a compensatory response it is certainly a very rapid one,

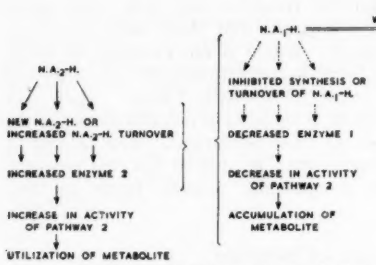


FIG. 2.—Possible mechanisms of stimulation of enzyme activity in virus-infected cells. (Key as for Fig. 1.)

and suggests either a high turnover rate of the enzyme or a very rapid transfer of information via level No. 3 above. The possible functions of this enzyme in alternative metabolic pathways are not understood, though a part in 2-carbon metabolism is suggested. Its elevation in mouse brain infected with a wide variety of neurotropic viruses as well as in ectromelia-infected mouse liver suggests a fundamental role in the process of virus multiplication.

This hypothesis has certain corollaries.

Host Specificity of Viruses.—This could be explained on the basis of structural similarity between the virus N.A. and the host cell N.A. A cell may be resistant to a virus either because of structural dissimilarity, so that competition does not occur; or because the host cell N.A. succeeds in the competition (possibly because of lower entropy).

Virus Ecology

For the purpose of this discussion the effect of host immunity due to antibody or other factors outside the potential host *cell* is ignored. There are several possible types of relationship between a virus and its host cell.

1. *Virus multiplication with cytopathic effect.*—This will be observed when key metabolic pathways are disturbed as a result of the virus succeeding in competition with the host. This may occur entirely because of a chance similarity between virus and host N.A. templates. The virulence of a virus could be due to the extent of the damage thus inflicted in terms of (*a*) numbers of key pathways involved; (*b*) the degree of damage to each particular pathway. Cytopathogenicity may also result from physical disorganization of a cell. This may in turn be the result of inhibition of synthesis of a structural protein either directly as a result of virus-host N.A. competition or indirectly as a result of metabolic damage.

2. *Virus multiplication without cell destruction* (for example, mumps virus in the amniotic cavity of the chick embryo).—This might be explained on the basis of competition between virus N.A. and host N.A. governing non-essential metabolic processes in the host.

3. *Persistence of virus in the host cell without multiplication and without damage to the cell.*—This possibility has been explored mainly in connexion with rabbit papillomatosis, and considerable doubt has been cast on its validity (Beard, 1956); it is not considered further here.

4. *Multiplication without cell destruction and with protection against other virus.*—This is one form of interference. The conditions governing its occurrence or the opposite phenomenon of dual infection are obscure. Henle *et al.* (1958) have described persistent infection of two lines of human cells with Newcastle disease, mumps, or 6–6 viruses without cytopathic effect and with protection against cytopathogenic influenza A (PR8), herpes simplex, and especially vesicular stomatitis viruses. Metabolic change occurred in the persistently infected tissue cultures in the form of increased aerobic glycolysis. Phenomena such as this represent a form of acquired cellular immunity. They might be explained as being due to the exclusion of a second virus N.A. by the first virus N.A., which has competed successfully with host N.A., the loss of which is non-lethal. Evidence for the involvement of N.A. in this type of interference is that 2,5-dimethylbenzimidazole, which inhibits N.A. synthesis and the multiplication of influenza virus, also prevents interference among various strains of the virus (Tyrrell and Tamm, 1955).

It is clearly not in the best interests of a virus to destroy its host. In the absence of a permanent supply of fresh susceptible hosts, changes in the character of a virus in the direction of decreased cytopathogenicity are likely to have considerable survival value. On the basis of the hypothesis above, these are likely to be changes in virus N.A. which allow it to replicate in competition with host N.A. without complete suppression of essential functions. Comparative studies of the effects of cytopathogenic and non-cytopathogenic viruses on the metabolism of similar host cells would obviously be of considerable interest in this respect.

Site of Damage in Ectromelia-Virus-Infected Mouse Liver

The accompanying Table shows alterations in levels of enzyme activity in all cell fractions except microsomes. Changes occur in the nucleus despite the apparent absence of viral material. In addition to the later biochemical changes, virus infection inhibits mitosis in regenerating liver as early as 10 hours after infection — that is, early in the eclipse phase (Miller and de Burgh, 1957). Ectromelia virus has not been analysed completely, but it is most likely that, as with the closely related vaccinia virus, its nucleic acid is deoxyribonucleic acid (D.N.A.). In the host cell, D.N.A. is overwhelmingly a nuclear component and is synthesized in the nucleus. However, the terminal stages of virus synthesis seem to occur in the cytoplasm, and metabolic changes occur in the cytoplasm. There is clearly a need to attempt to detect viral D.N.A. in the nucleus in the earliest stages of infection. This is likely to present considerable technical difficulties, as even with a high virus:cell ratio the amount of virus entering the cell is only 0.0004 of the total cell volume.

"Virus Metabolism" and Carcinogenesis

The ability of some viruses to cause neoplastic growth in undoubted. Of much less certainty are the following questions: Is this a direct result of virus infection? if so, What is the mechanism of production of the neoplastic change? and What is the relation of the process of virus multiplication in general to the process of neoplasia? In a review of tumour-virus problems Furth and Metcalf (1958) discuss three theories of the action of viruses in causing neoplasms: conditioning, mutation, and transduction. By conditioning is meant some correctable disturbance in the forces regulating or influencing the growth of a cell; it is suggested that a tumour virus may interfere with the production of a growth-regulating substance and that such cells might then multiply unrestrained, or that the virus prevents the cell from responding to normal extrinsic control. It is

also suggested that tumour viruses cause a "somatic mutation" or are genic material derived from neoplastic or potentially neoplastic cells and act in a manner analogous to the transduction of bacteria.

It is convenient to view neoplastic transformation of a cell as involving both a metabolic change—possibly a depletion of some enzymes (Potter, 1958)—and a change in its surface character. The former would release the cell from general growth-restriction and the latter would release it from local controls of the type visualized by Weiss (1947). In considering the relation between viruses and neoplasia there are two fundamental questions: (1) Do these changes occur in cases of infection by known tumour viruses? and (2) Can analogous changes be induced in other cells by other viruses which do not cause tumours? There appears at the moment to be a presumptive "yes" to the first question. The changes observed in ectromelia-infected mouse liver appear highly relevant to the second.

In ectromelia-infected mouse liver there occur both an abnormal form of growth and metabolic changes which are in some respects similar to those observed in hepatic neoplasms. Though abnormal growth is cytoplasmic and not nuclear, and though these changes are acute and followed by cell-death, there are obvious parallels. Whether one calls the process conditioning, mutation, or transduction, there is a possibility that at least some of the metabolic changes underlying neoplasia result from competition between host cell and foreign ("virus") N.A.

Tumour viruses with a short latent period, such as the Friend agent (Metcalf *et al.*, 1959), would produce all the necessary changes. Tumour viruses with a long latent period would require additional processes for the production of some changes, made possible by the initial viral competition. The retention of such changes in daughter cells requires comment. If the virus remains present at an unaltered concentration in each cell the direct competition theory is relevant. If the amount of virus decreases, as it apparently does in, for example, the Rous sarcoma (Groupé and Rauscher, 1957) or Shope papilloma (Greene, 1953) virus tumours, then additional mechanisms must be invoked. Virus N.A. may persist and be passed on from cell to daughter cell, though in a form or in quantities not demonstrable by current techniques.

In other "spontaneous" neoplasms some at least of the changes involved may be due to several more or less chance competitions of this type, no single one of which is adequate to produce either neoplasia or other recognized defect. Non-viral tumours would appear compatible with this thesis. Direct damage to cell N.A. by—for example, ionizing radiation or alteration of cell N.A. synthesis by chronic inflammation, could institute stepwise alterations of metabolism leading to neoplastic transformation.

Somewhat similar views on virus multiplication (Gottschalk, 1957) and carcinogenesis (Potter, 1958) have been expressed by other writers. There has, however, always been a gap between observed facts in regard to either virus multiplication or cancer metabolism and the mechanisms proposed to explain them. The observations of an association between virus multiplication, metabolic changes, and abnormal or unbalanced growth in ectromelia-infected mouse liver may help to fill this gap.

Enzyme Levels in Virus-infected, Neoplastic, and Other Tissues

Tissue	Enzyme								
	Nuclear		Mitochondrial	Lysosomal				Microsomal	Soluble
	D.P.N. Synthesis	Adenosine Deaminase	Succinic Dehydrogenase and Mitochondria	Uricase	Acid Phosphatase	Cathepsin	Catalase	Glucose-6-phosphatase	Xanthine Oxidase or Dehydrogenase
Ectromelia-infected mouse liver	−[10]	−[12]	+[19]	±[19]	−[19]	−[11]	±[11]	±[11]	+[19]
Other virus-infected tissues		+ (Neurotropes in mouse brain)[5]	Variable[4,8,14]		− (Polio-virus in monkey kidney;[18] ± (Bunyamwera in Ehrlich ascites. Carcinoma)[9]	− (Coxsackie in HeLa)[9]			+ (Neurotropes in mouse brain)[6] − (Bunyamwera in Ehrlich ascites)
Regenerating liver	−[10]	− (late)[12]	−[1, 20, 25]	−[19]	±[19]			±[26]	+[15, 19]
Precancerous liver (azo-dye)			− (Mitochondria)[3]	±[21]	−[3]			−[27]	−[20]
Azo-hepatoma	−[16]	±[20] +[13]	− (Mitochondria and enzyme)[3, 22]	±[21]	−[3]			−[27]	−[20]
Spontaneous hepatoma	−[16]		− (Mitochondria)[3]	−[13]	±[3]	±[3]			−[17]
Transplanted hepatoma			−[22]		−[3]	−[3]		Nil[27]	
Livers of tumour-bearing animals	− (Leukaemia) ± (Solid tumour)[23]			−[24]			−[3]	−[27]	
Foetal liver	−[7]							−[28]	−[17]
Livers of starved animals			− (Proportional to loss of cytoplasm)[2]	− (Proportional to loss of cytoplasm)[2]	+[3]	− (Proportional to loss of cytoplasm)[2]			− (Not proportional to loss of cytoplasm)[2]

\+ Increase. ± No change. − Decrease.

[1] Allard *et al.* (1952).
[2] Allard *et al.* (1957a).
[3] Allard *et al.* (1957b).
[4] Bauer (1947).
[5] Bauer (1951).
[6] Bauer and Bradley (1956).
[7] Branster and Morton (1956).
[8] Colter *et al.* (1957).
[9] Crowell and Syverton (1958).
[10] de Burgh (1957).
[11] d: Burgh (unpublished results).
[12] d: Burgh and Nelson (unpublished results).
[13] d: Lamirande and Allard (1957).
[14] de Ritis *et al.* (1957).
[15] Feigelson *et al.* (1957).
[16] Glock and McLean (1957).
[17] Greenstein (1954).
[18] Kovacs (1956).
[19] Nelson and de Burgh (1959).
[20] Reid and Lewin (1957).
[21] Schneider *et al.* (1953).
[22] Schneider and Potter (1943).
[23] Shuster *et al.* (1958).
[24] Thomson and Klipfel (1958).
[25] Tsuboi *et al.* (1951).
[26] Weber and Cantero (1955a).
[27] Weber and Cantero (1955b).

Summary

Ectromelia (mouse-pox) virus multiplying in mouse liver provides an excellent model for the study of the effect of a virus on the metabolism of its natural mammalian-host cell. In this host–virus system metabolic changes are accompanied by "unbalanced" (purely cytoplasmic) growth of the cell. Some metabolic changes occurring in this system are compared with those occurring (*a*) in other virus-infected tissues; (*b*) in regenerating liver showing "balanced" (nuclear and cytoplasmic) growth; (*c*) in precancerous and cancerous livers showing abnormal growth; (*d*) in the livers of tumour-bearing animals; and (*e*) in the livers of embryonic and starved animals. No consistent pattern of changes of enzyme activities is observed in either virus-infected or neoplastic tissues, nor are the changes similar to those in the livers of embryonic or starved animals.

A possible mechanism is suggested for the production of metabolic changes in virus-infected tissues. It is proposed that such changes occur as the result of more or less chance competition between virus nucleic acids and structurally similar host-cell nucleic acids which control, or form templates for, the synthesis of host enzymes. Some implications of this explanation are discussed with regard to various host–virus relationships.

Since virus infection, metabolic change, and unbalanced cell growth may be associated, the hypothesis of nucleic-acid competition is considered in relation to neoplasia. Neoplastic transformation may involve a metabolic change and a change in surface character; both these changes clearly could be the result of a process similar to that occurring in virus infection. The lack of pattern in enzyme changes in various hepatic neoplasms may be the outcome of chance competitions between foreign nucleic acid and host-cell nucleic acid, some of which may be quite incidental to the underlying primary changes characteristic of neoplasia. This hypothesis is discussed in relation to the causation of tumours by known tumour-viruses and to "spontaneous" neoplasms, in which at least some of the alterations involved may be due to nucleic-acid competitions.

The experimental work referred to above has been supported by a grant from the National Health and Medical Research Council of Australia and was carried out in part during the tenure by one of us (D.S.N.) of a British Medical Association Ordinary Research Scholarship. We thank Mrs. I. M. Stephens for technical assistance.

REFERENCES

Allard, C., de Lamirande, G., and Cantero, A. (1952). *Cancer Res.*, **12**, 580.
—— —— —— (1957a). *Exp. Cell. Res.*, **13**, 69.
—— —— —— (1957b). *Cancer Res.*, **17**, 862.
Bauer, D. J (1947). *Brit. J. exp. Path.*, **28**, 440.
—— (1951). Ibid., **32**, 7.
—— (1953). In *The Nature of Virus Multiplication: 2nd Symposium of the Society for General Microbiology, Oxford, 1952*, p. 46. University Press, Cambridge.
—— and Bradley, P. L. (1956). *Brit. J. exp. Path.*, **37**, 447.
Beard, J. W. (1956). *Cancer Res.*, **16**, 279.
Branster, M. V., and Morton, R. K. (1956). *Biochem. J.*, **63**, 640.
Burnet, F. M. (1956). *Enzyme, Antigen and Virus*. University Press, Cambridge.
Colter, J. S., Bird, H. H., and Koprowski, H. (1957). *Cancer Res.*, **17**, 815.
Crowell, R. L., and Syverton, J. T. (1958). *Fed. Proc.*, **17**, 508.
de Burgh, P. M. (1957). *Aust. J. Sci.*, **20**, 86.
de Lamirande, G., and Allard, C. (1957). *Proc. Amer. Ass. Cancer Res.*, **2**, 224
de Ritis, F., Coltorti, M., and Giusti, G. (1957). *J. infect. Dis.*, **101**, 219.
Feigelson, M., Feigelson, P., and Gross, P. R. (1957). *J. gen. Physiol.*, **41**, 233
Furth, J., and Metcalf, D. (1958). *J. chron. Dis.*, **8**, 88.
Glock, G. E., and McLean, P. (1957). *Biochem. J.*, **65**, 413.
Gottschalk, A. (1957). *Physiol. Rev.*, **37**, 66.
Green, H. N. (1954). *Brit. med. J.*, **2**, 1374.
Greene, H. S. N. (1953). *Cancer, Res.*, **13**, 726.
Greenstein, J. P. (1954). *Biochemistry of Cancer*. 2nd ed. Academic Press, New York.
Graupé, V., and Rauscher, F. J. (1957). *Science*, **125**, 694.
Henle, G., Deinhardt, F., Bergs, V. V., and Henle, W. (1958). *J. exp. Med.*, **108**, 537.
Kovacs, E. (1956). Ibid., **104**, 589.
Metcalf, D., Furth, J., and Buffett, R. J. (1959). *Cancer Res.*, **19**, 52.
Miller, J. F. A. P., and de Burgh, P. M. (1957). *Aust. J. exp. Biol. med. Sci.*, **35**, 115.
Nelson, D. S., and de Burgh, P. M. (1958). Ibid., **182**, 1617.
—— —— (1959). *Virology*, **9**, 127.
Potter, V. R. (1958). *Fed. Proc.*, **17**, 691.
Reid, E., and Lewin, I. (1957). *Brit. J. Cancer*, **11**, 494.
Schneider, W. C., Hogeboom, G. H., Shelton, E., and Striebich, M. J. (1953). *Cancer Res.*, **13**, 285.
—— and Potter, V. R. (1943). Ibid., **3**, 353.
Shuster, L., Langan, T. A., Kaplan, N. O., and Goldin, A. (1958). *Nature (Lond.)*, **182**, 512.
Thomson, J. F., and Klipfel, F. H. (1958). *Cancer Res.*, **18**, 229.
Tsuboi, K. K., Stowell, R. E., and Lee, C. S. (1951). Ibid., **11**, 87.
Tyrrell, D. A. J., and Tamm, I. (1955). *J. Immunol.*, **75**, 43.
Weber, G., and Cantero, A. (1955a). *Cancer Res.*, **15**, 679.
—— —— (1955b). Ibid., **15**, 105.
Weiss, P. (1947). *Yale J. Biol. Med.*, **19**, 235.

RIGHT HEMIHEPATECTOMY FOR PRIMARY HEPATOMA

WITH SPECIAL REFERENCE TO DIAGNOSIS AND BIOCHEMICAL CHANGES

BY

A. OTAKI, M.B., M.R.C.P.

Lecturer in Chemical Pathology, St. George's Hospital, London

A. E. READ, M.D., M.R.C.P.

Senior Registrar and Tutor in Medicine, Department of Medicine, Postgraduate Medical School of London, Hammersmith

J. STUBBS, M.B., B.S., Ph.D.

Surgical First Assistant, St. George's Hospital, London

AND

H. SCULTHORPE, F.I.M.L.T.

Senior Technician, Department of Clinical Pathology, St. George's Hospital, London

The surgical removal of the right lobe of the liver is a rare event. It has been performed for cysts and primary tumours confined to the right lobe, for carcinoma of the gall-bladder, for hepatic abscess, and for injuries to the liver, and may sometimes be indicated when the right lobe is the site of secondary neoplasm.

The following report describes some of the diagnostic, surgical, and biochemical features of a case in which the operation was performed for a primary malignant tumour of the liver.

Case Report

A schoolgirl now aged 14, with no previous medical history, began to have attacks of vomiting in 1957. On admission to hospital after a minor abdominal injury she was found to have gross hepatosplenomegaly. Investigation was unrewarding, and in March, 1958, laparotomy was performed. The hepatosplenomegaly was confirmed; the liver, though enlarged, looked normal; and liver biopsy showed normal liver tissue only.

Subsequently ascites and ankle oedema developed and the patient's condition deteriorated. In January, 1959, she was

referred to Hammersmith Hospital for further investigation under the care of Dr. Sheila Sherlock.

Physical examination revealed a wasted, ill-looking girl with ascites and anaemia (Fig. 1). The enlarged liver was firm, with a smooth surface 5 in. (12.5 cm.) below the right costal margin, and the spleen extended 4 in. (10 cm.) below the left costal margin. There were no cutaneous stigmata of chronic liver disease and no enlarged lymph nodes. Rectal examination was normal.

Investigations (January, 1959).—Weight 6 st. 6 lb. (40.8 kg.). Haemoglobin, 8.8 g. (60%); M.C.H.C., 31.5%; W.B.C., 7,000/c.mm. (normal differential count); platelets normal. Urine, protein present (84 mg./100 ml.). Tests for occult blood in stools negative; serum electrolyte levels normal; blood urea, 34 mg./100 ml.; W.R. and Kahn test negative. Liver-function tests: bilirubin, 0.2 mg./100 ml.; cholesterol, 166 mg./100 ml.; alkaline phosphatase, 15 K.-A. units; thymol turbidity, 1 unit; zinc sulphate, 0 unit; prothrombin time, 15 sec. (control time, 12 sec.); transaminases—G.O.T. 19 units/ml., G.P.T. 9 units/ml.; total protein, 6.6 g./100 ml. (albumin 3.4 g. (later falling to 1.9 g.), globulin, 3.2 g.). Electrophoresis showed an increase of alpha$_2$- and beta-globulins (see Fig. 5). Serum iron, 38 mg./100 ml. Examination of the sternal marrow showed a hypercellular marrow with evidence of iron deficiency. Coombs test negative; L.E. cells not seen. There was moderate generalized aminoaciduria. The serum copper oxidase was normal. The ascitic fluid was clear and straw-coloured. No cancer cells or tubercle bacilli were found in it.

FIG. 1.—Patient before operation, showing abdominal distension due to hepatosplenomegaly and ascites and the marked degree of muscle-wasting.

X-ray examination: the chest film showed no abnormality apart from a small right pleural effusion; barium meal examination revealed no abnormality in the stomach and there were no oesophageal varices; and bone films were normal.

At this stage, the condition still undiagnosed, repeat liver biopsy and a portal splenogram were performed under general anaesthesia. The portal splenogram showed normal splenic and portal-vein filling (Fig. 2) and normal filling of the left lobe of a greatly enlarged liver. On the right side, vessels were absent and neighbouring portal radicles were displaced medially. These appearances were suggestive of a large tumour in the right lobe of the liver. Needle biopsy of the liver obtained by the intercostal route, from the area corresponding to the filling defect, yielded a white and friable tissue whose neoplastic character was confirmed by microscopy. This revealed an anaplastic tumour suggestive of a primary hepatoma.

The patient was referred to Mr. Rodney Smith at St. George's Hospital for surgical removal of the tumour, a procedure which, though formidable, was considered to be a worth-while risk.

Operation.—This was performed on February 23, 1959. The approach was essentially that of Pack and Baker (1953). A long right paramedian abdominal incision was made. The right lobe of the liver was found to be greatly enlarged and splenomegaly was present. An adhesion joining the liver

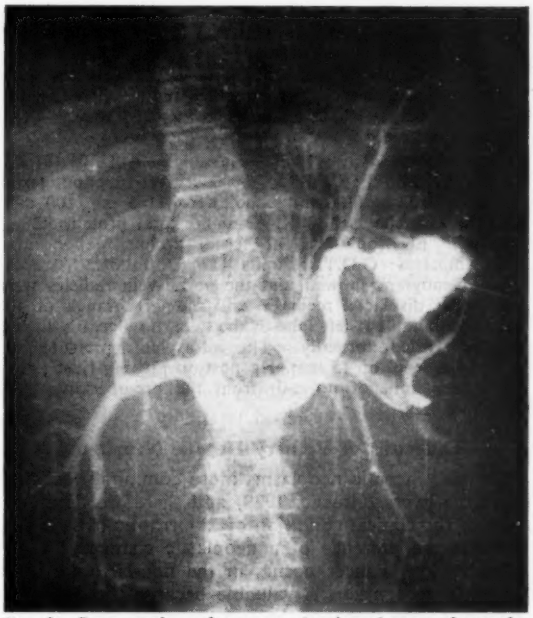


FIG. 2.—Pre-operative splenogram, showing absence of vascular filling in right lobe of liver, compression of vessels in left lobe, and widening of portal-vein bifurcation.

to the diaphragm at one point was resected later with the right lobe. Since the thoraco-abdominal approach allows the liver to be herniated into the thorax and permits a good view of the porta hepatis, the ninth costal cartilage was divided, the abdominal incision extended into the intercostal space, and the diaphragm split towards the inferior vena cava. After identification of the structures of the porta hepatis, a formal right hemihepatectomy was performed, using the technique described by Rodney Smith (1958). The diaphragm was reconstituted and the wound closed, leaving two corrugated drains from the liver and a water-seal drain from the chest.

The specimen weighed 1,860 g. and contained a solitary tumour 15 cm. in diameter, surrounded by a false capsule of liver tissue (Fig. 3). The line of section was beyond the tumour margin. The microscopical appearance was that of a malignant hepatoma. The low mitotic rate and the degree of differentiation indicated a slowly growing tumour.

FIG. 3.—Specimen removed at operation, consisting of right lobe of liver and the tumour (about 15 cm. in diameter), which is surrounded by a false capsule of normal liver tissue.

Post-operative Management.—The chest drain was removed after 24 hours. Intravenous therapy with 4.3% dextrose in 0.18 N saline was continued for four days. In addition, three albumin infusions were given (total 75 g.). Vitamin K, 10 mg. intramuscularly, was given daily for seven days. Two days after operation the patient became pyrexial, and eight days later a right subphrenic abscess was opened and drained. The abscess persisted, but after being reopened three weeks later her further recovery was uneventful.

Follow-up.—The patient was readmitted to hospital six months after operation for reassessment. On examination she showed a vast improvement in physical status. There was some clinical enlargement of the left lobe of the liver, and the spleen, though just palpable, was much reduced in size. She weighed 6 st. 12 lb. (43.5 kg.) and was about to return to school.

Investigations (July, 1959).—Haemoglobin 12 g. (81%); M.C.H.C., 31.5%; W.B.C., 6,000 Liver-function tests: bilirubin, 0.3 mg./100 ml.; cholesterol, 165 mg./100 ml.; alkaline phosphatase, 18 K.-A. units; total protein 7.2 g./100 ml. Electrophoresis of serum protein was normal. Transaminases: G.O.T. 16 units, G.P.T. 10 units. A repeat portal venogram showed that the portal-vein radicles were no longer displaced medially and the left branch of the portal vein and the left lobe of the liver, now greatly hypertrophied, filled normally. The intrasplenic pressure had risen to a level of 15 mm. Hg post-operatively (just above the upper limit of normal) from the pre-operative level of 6 mm. Hg.

Diagnosis of Primary Hepatic Neoplasms

Primary hepatic neoplasms more commonly occur in cirrhotic livers (Greene, 1939) and therefore deterioration of the clinical condition of a cirrhotic patient may indicate the presence of a neoplastic change. When primary liver cancer occurs in the non-cirrhotic liver, its early recognition is valuable because the patient is usually young, because the tumour may be slow to metastasize, and because, with modern technique, the surgical risk in itself is not too great.

Some diagnostic points of possible importance arising from a comparison of this case with other cases are: the serum electrophoretic pattern; the serum alkaline phosphatase; splenic portal venography and liver biopsy; and ascites.

Serum Electrophoretic Pattern.—Six patients with primary hepatic neoplasms seen at Hammersmith Hospital in the past three years have shown the same serum protein abnormality on electrophoresis. The alpha$_2$- and beta-globulins were increased, in contrast to the usual gamma-globulin increase seen in hepatic cirrhosis. It seems, therefore, that in a young person with unexplained hepatomegaly this alteration in serum protein justifies a vigorous attempt to exclude a primary liver neoplasm, including the use of splenic portal venography.

Serum Alkaline Phosphatase.—That malignant hepatoma need not be accompanied by abnormal liver-function tests, and in particular abnormal alkaline phosphatase and transaminase levels, is proved by the findings possible in this case. Nevertheless, helpful collateral evidence of an intrahepatic space-occupying lesion is provided by a raised serum alkaline phosphatase, provided bone disease and obstructive jaundice are absent. In four of the six cases the alkaline phosphatase was raised (22–102 K.-A. units), but in the present case and one other the levels were normal for the patient's age.

Splenic Venography and Liver Biopsy.—Bergstrand and Elkman (1955) have shown that splenic portal venography can be used to demonstrate primary and secondary tumours of the liver. Venography in our patient defined the extent of the lesion, but also indicated that as the left lobe was unaffected the condition was suitable for surgery. Early venography may produce the evidence of a deep-seated space-occupying lesion which biopsy may be unable to supply. Thus nine months after a negative operative biopsy, needle biopsy yielded pathological tissue from a tumour which must have enlarged in the interim.

Ascites.—Since ascites was present for some time before the patient's admission to Hammersmith Hospital, despite normal total serum proteins, it was logical to consider the possibility of peritoneal involvement by the tumour. It is therefore important to recognize that in such a case ascites is not necessarily a sign of inoperability. The cause of the splenomegaly is unknown, for it was not due to portal hypertension or involvement by tumour.

Biochemical Changes

Serum bilirubin and Alkaline Phosphatase

Frequent liver-function tests and serum bilirubin, cholesterol, and transaminase estimations were made

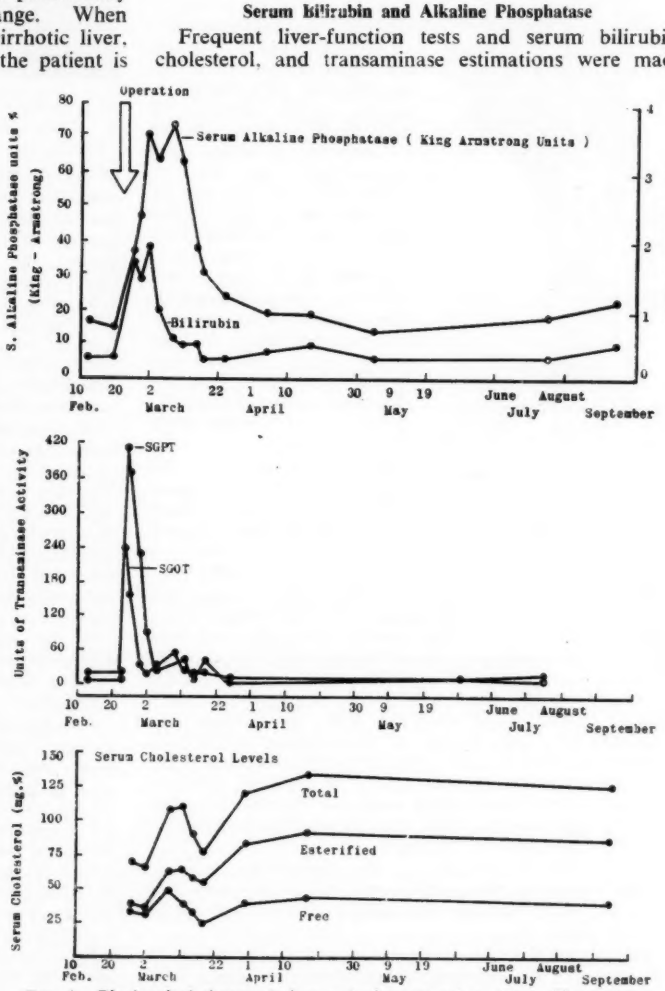


FIG. 4.—Biochemical changes before and after operation. Top: The serum alkaline phosphatase and bilirubin values. Middle: The serum glutamic oxalacetic transaminase (S.G.O.T.) and serum glutamic pyruvic transaminase (S.G.P.T.) values. Bottom: The total, esterified, and free cholesterol values.

after the operation. Fig. 4 (top graph) relates serum bilirubin to alkaline phosphatase. Both show a rapid post-operative rise, with curves of the same general character. The bilirubin did not exceed 1.9 mg./100 ml. despite blood transfusion, but the alkaline phosphatase rose to 75 units (K.-A.). The bilirubin returned to normal (0.6 mg./100 ml.) by the twenty-fourth day, whereas the alkaline phosphatase remained above normal (18–20 K.-A. units at 14 years) until the forty-first post-operative day.

Figures published by Califuno *et al.* (1958), after partial hepatectomy in rabbits, show that the alkaline phosphatase rose from three to nine times the pre-operative level in two days and regained initial levels by the eighteenth day. After partial hepatectomy in rats the regenerating cells are reported to be rich in alkaline phosphatase, at a time when the blood levels are also high (Rosenthal *et al.*, 1952). However, incomplete biliary obstruction is also associated with high alkaline phosphatase values, out of proportion to the serum bilirubin (Sherlock, 1958), and congestive hepatic changes due to increased portal blood-flow through the remaining lobe of the liver may account for serum bilirubin and phosphatase findings in this case. Evidence for the presence of these changes after partial hepatectomy has been shown in dogs (Mazzec *et al.*, 1957). Six and eight months after surgery the serum alkaline phosphatase and bilirubin were 18 and 22 units and 0.3 mg. and 0.5 mg./100 ml. respectively.

Serum Transaminase

Serum transaminase levels (Fig. 4, middle graph), which were normal pre-operatively, rose steeply immediately afterwards to 420 S.G.P.T. units and 240 S.G.O.T. units respectively, and fell precipitously to the normal region (below 40 units) within 10 days. They represent extensive but finite tissue damage and cannot be related to liver-cell regeneration.

Slight elevations above the normal upper limit occurred later but without correlating with the clinical and surgical events connected with a subphrenic abscess present at the same time.

In July, 1959, the results were 10 S.G.P.T. units and 14 S.G.O.T. units respectively.

Serum Cholesterol

Fig. 4 (bottom graph) illustrates the changes in serum cholesterol after surgery. Pre-operative values of 161 mg. and 166 mg./100 ml. were obtained by Zak's ferric chloride method (Zak, 1957), which gives consistently higher results than Sperry's digitonin method (Schoenheimer and Sperry, 1934), used to derive the values for the graph shown.

Initial post-operative readings, even allowing for the expected difference, were unaccountably low. Total cholesterol on the first and sixth post-operative days were 72 mg. and 65 mg./100 ml. respectively. Such low values are associated usually with severe wasting disease, anaemia, hyperthyroidism, and acute infection. Prolonged malnutrition certainly characterized this case, but as pre-operative cholesterol values were normal, and as malnutrition is associated with a reduction in plasma volume (Denz, 1947; Walters *et al.*, 1947), it is more likely that the decrease was due to re-expansion of the plasma volume in response to parenteral therapy. During the operation 5 pints (2,840 ml.) of blood was transfused, and in the next three days the patient received 75 g. of albumin. A week after operation the total cholesterol rose steeply from 65 mg. to 110 mg./100 ml., and during the next 17 days subsided to 77 mg./100 ml. This increase did not begin until the transient bilirubin elevation had passed its peak. These changes could be due to intrahepatic biliary obstruction associated with hepatic congestion (Mazzec *et al.*, 1957), but why there was a lag between the cholesterol and bilirubin peaks is difficult to explain.

The percentage of esterified cholesterol, at first subnormal (53% of total; normal 60–80%), began to increase despite the presumed obstructive process. By the twenty-second day after operation, though the total was still low (90 mg./100 ml.), the percentage of esterified cholesterol had become normal (63%). It seems, then, that in regard to cholesterol a moderate degree of intrahepatic obstruction has a mechanical effect upon the serum cholesterol level but not a functional effect upon liver cholesterol metabolism.

The general rise in cholesterol level continued. At discharge in May, 1959, the total was 128 mg./100 ml., and five months later it was 125 mg./100 ml., with 69% as esterified cholesterol. The total cholesterol by an alternative method was 165 mg./100 ml. These results are within the normal range for the methods used.

Serum Proteins

The patient suffered progressive anorexia, and her nutrition had been poor for many months, as the pre-operative photograph clearly shows. In the month before operation the serum albumin fell from 3.4 g. to 1.9 g./100 ml., reducing the total protein to 4.7 g./100 ml.

It is widely agreed that tissues in general undergo severe protein depletion before the plasma protein is reduced to any great extent. In our patient, undernourished for so long, tissue depletion is assumed to have reached a critical degree. Continued tumour growth, ascites formation, and decreasing protein intake may have tipped the negative nitrogen balance to the point at which the serum albumin would be greatly reduced.

During the operation 5 pints (2,840 ml.) of blood was transfused, followed over the next three days by 75 g. of purified human albumin. At the end of this time the total protein was 7.1 g./100 ml. (albumin 3.5 g.). But thereafter the albumin fell continuously until the twelfth day to 1.8 g./100 ml., a fall largely masked in the total protein levels by a simultaneous increase in the globulins to 4.5 g. from 2.8 g./100 ml.

The albumin then rose slowly, and by the fortieth day the total protein was 7.6 g. and the albumin 3.5 g./100 ml.

The electrophoretic analyses (Fig. 5) indicate some of the changes discussed above. They show, too, the alpha$_2$- and beta-globulin increase referred to in discussing diagnosis. These changes commonly occur in nephrosis, therefore it is not surprising that their occurrence in six cases of primary hepatic tumour should raise the question of their diagnostic value. The alpha- and beta-globulin together form about 17% of the total serum proteins and are largely concerned with the carriage of various substances about the body. Kekwick (1956) related the raised beta-globulin in nephrosis to the high cholesterol levels found in that condition. In our case, since both serum cholesterol and serum bilirubin were normal pre-operatively, it was not possible to account for the globulin changes in the same way.

The increase in alpha$_2$- and beta-globulin may, of course, be a specific response to a hepatic neoplasm or even the product of the tumour's own metabolism, but the possible effects of hypoalbuminaemia and malnutrition must be taken into account before seriously considering that this is the case. Thus Gutman (1948) states that an alpha-globulin increase occurs almost constantly when albumin levels are lowered, except in many cases of multiple myeloma. Chow *et al.* (1945), examining the effects of starvation in dogs, found that despite a marked loss of albumin and a slight decrease in gamma-globulin alpha-globulin tended to rise. Kekwick (1951) noted increased serum globulin in human malnutrition, unassociated with a particular constituent. Certainly, however, an alpha- and beta-globulin increase may help to distinguish hepatic neoplasm from hepatic cirrhosis and other causes of hepatomegaly, and in appropriate cases their occurrence will warrant the inclusion of a hepatic neoplasm in the differential diagnosis.

After operation serum electrophoresis showed a peak of alpha-globulin (Fig. 5), and Schiff's reaction on a series of strips (McGuckin and McKenzie, 1958) showed that the increase was in the glycoprotein fraction. The alpha peak then subsided, but alpha$_2$-globulin did not predominate again until the twenty-fourth day after operation. Califano *et al.* (1956) has also noted a moderate increase in alpha$_1$- and beta-globulins after partial hepatectomy in animals.

When the patient was discharged in May, 1959, serum electrophoresis was normal except for a moderate increase in gamma-globulin (total protein, 7.2 g./100 ml. (albumin 3.3 g.)).

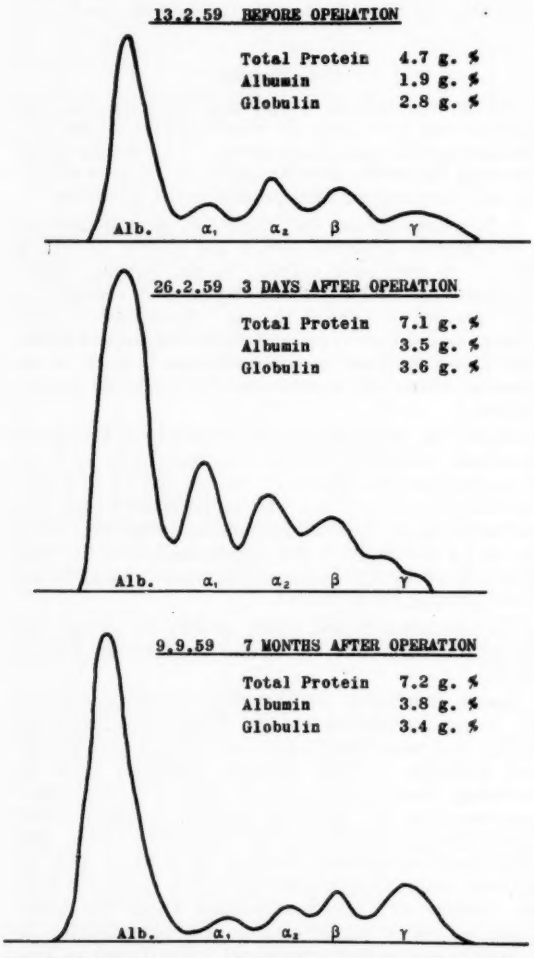

13.2.59 BEFORE OPERATION
Total Protein 4.7 g. %
Albumin 1.9 g. %
Globulin 2.8 g. %
Alb. α1 α2 β γ
26.2.59 3 DAYS AFTER OPERATION
Total Protein 7.1 g. %
Albumin 3.5 g. %
Globulin 3.6 g. %
Alb. α1 α2 β γ
9.9.59 7 MONTHS AFTER OPERATION
Total Protein 7.2 g. %
Albumin 3.8 g. %
Globulin 3.4 g. %
Alb. α1 α2 β γ

FIG. 5.—Changes in serum electrophoretic pattern. Top: Before operation, showing an α_2-β-globulin increase. Middle: Three days after operation, showing a predominant increase in α_1-globulins. (Excessive background altered the globulin baseline.) Bottom: Seven months after operation. The pattern is normal.

Summary

The clinical features produced by a primary hepatic neoplasm (hepatoma) in a patient aged 13 years are described, together with an account of the diagnostic problems it presented. The value of portal splenography in the diagnosis of hepatic tumours is stressed and evidence is presented to suggest that consideration of the electrophoretic pattern (which may show on α_2-β peak in each case) may be of value.

The biochemical changes resulting from removal of the right lobe of the liver in this patient are described. The noticeable features were a marked rise in the serum alkaline phosphatase and transaminases, accompanied by a slow rise in the serum cholesterol and its esterified fraction. The significance of these changes is discussed.

To Professor Sheila Sherlock, Mr. Rodney Smith, and Professor N. Martin we wish to express our thanks for their help and advice, and permission to publish. To Professor Sherlock and Dr. D. N. S. Kerr we are indebted for the collection of information on patients with primary hepatic tumours seen at Hammersmith Hospital.

REFERENCES

Bergstrand, I., and Ekman, C.-A. (1955) *Acta radiol. (Stockh.)*, **43**, 377.
Califano, G., Iovino, M. G., and Schiano, S. (1956). *G. ital. Chir.*, **12**, 794.
—— Teramo, A., and Schiano, S. (1958). *Athena (Roma)*, **24**, 116.
Chow, B. F., Allison, J. B., Cole, W. H., and Seeley, R. D. (1945). *Proc. Soc. exp. Biol. (N.Y.)*, **60**, 14.
Denz, F. A. (1947). *Quart. J. Med.*, **16**, 1.
Greene, J. M. (1939). *Int. Abstr. Surg.*, **69**, 231.
Gutman, A. B. (1948). *Advanc. Protein Chem.*, **4**, 155.
Kekwick, R. A. (1951). *Rep. Ser. med. Res. Coun. (Lond.)*, No. 275, p. 207.
—— (1956). *Lectures on the Scientific Basis of Medicine, 1954–55*, **4**, 112. Athlone Press, London.
McGuckin, W. F., and McKenzie, B. F. (1958). *Clin. Chem.*, **4**, 476.
Mazzeo, F., Conti, A., and Visconti, S. (1957). *G. ital. Chir.*, **13**, 293.
Pack, G. T., and Baker, H. W. (1953). *Ann. Surg.*, **138**, 253.
Rosenthal, O., Fahl, J. C., and Vars, H. M. (1952). *Amer. J. Physiol.*, **171**, 604.
Schoenheimer, R., and Sperry, W. M. (1934). *J. biol. Chem.*, **106**, 745.
Sherlock, S. (1958). *Diseases of the Liver and Biliary System*, 2nd ed., p. 25. Blackwell, Oxford.
Smith, R. (1958). In *Operative Surgery; Progress Volume 1958*, edited by C. Rob and R. Smith, p. 48. Butterworth, London.
Walters, J. H. Rossiter, R. J., and Lehmann, H. (1947). *Lancet*, **1**, 244.
Zak, B. (1957). *Amer. J. clin. Path.*, **27**, 583.

After the fourth teratology conference, which was held recently at the Memorial Sloan-Kettering Cancer Centre in New York City and attended by 76 scientists from Canada, England, France, Germany, and the U.S.A., the Teratology Society was formed with the aim of holding regular meetings in which investigations concerned with the aetiology and morphogenesis of congenital malformations could be presented and discussed. Inquiries about the Society should be sent to Dr. Marjorie M. Nelson, Department of Anatomy, School of Medicine, University of California, San Francisco, 22, California, U.S.A.

THE PREVENTION OF POST-OPERATIVE OEDEMA

CONTROLLED CLINICAL TRIAL OF LYOPHILIZED CHYMOTRYPSIN IN PLASTIC SURGERY

BY

JAMES CALNAN,* F.R.C.S.

AND

A. BARR, M.Sc.

From the Churchill Hospital and the Oxford Regional Hospital Board, Oxford

Much of the post-operative care of wounds in plastic surgery is directed toward the prevention of oedema. It is no longer felt that post-operative swelling should be a necessary sequel to successful surgical treatment, and to both surgeon and patient such swelling is a nuisance. The suggestion that oedema could be prevented, or at least mitigated, by therapy before operation is attractive, and there can be little doubt that such would have wide and immediate application. Though oedema appears to be related to the type and severity of the operative trauma, the teleological causes and the exact mechanism of production are still largely unknown. For this reason little success has followed the use of drug therapy. Lyophilized chymotrypsin ("chymar") has been heralded as one successful agent, and after the enthusiastic report of its use in plastic surgery by Moore (1959) a critical evaluation of this preparation seemed worth while.

Material and Methods

Because of the difficulty in assessing the presence or absence of post-operative swelling in certain regions of the body, cases admitted to the trial were limited to patients who were having operations on parts of the body where swelling after operation is either common or at least easily discernible. The way in which tne cases were grouped is shown in Table I.

TABLE I.—*Type of Operation in 56 Patients in Trial*

Type of Surgery	No. of Patients
Eyelid	4
Flaps, either tubed or direct	10
Hypospadias repair	16
Face-lift and major operations on the face	12
Nose reductions	14

The chymar was supplied lyophilized in the dry state in unlabelled ampoules of 5,000 units, in which state it will keep indefinitely. The dummy ampoules contained gelatin hydrolysed, 0.6 mg., and lactose, 5.4 mg. The diluent, normal saline, was supplied in 1-ml. phials. All the ampoules were delivered to the hospital pharmacist in bulk, the boxes containing them being clearly labelled, but all individual ampoules were unlabelled. Patients on chymar received 10,000 units in 2 ml. of fluid intramuscularly one hour before operation, and a similar dose on each of the two following days: those on the dummy ampoules received 2 ml. of the innocuous solids at similar times.

Patients were admitted in rotation from the hospital waiting-list, and, if thought medically suitable for entry into the trial, a standard prescription was sent to the hospital pharmacy. The trial was organized on the double-blind technique. This means that for each patient treated with the drug a control patient was given the dummy, so that surgeons and nurses were unaware which treatment was given to the patients until after the trial was completed. The treated and untreated series were matched for type of surgery (Table I). Chymar and the dummy were given to each pair, the allocation being made by the pharmacist by tossing a coin.

Though the surgical operations were performed by three surgeons, assessments were made by one of us (J. C.) and recorded on a standard form.

The trial was arranged so that it could be analysed sequentially. On this basis it is possible to assess the significance of the results as they become available, and the trial is terminated or continued according to the results already obtained. However, owing to the limited quantity of drugs available, the number of patients in the trial was inadequate to complete the original sequential analysis. Therefore the results are presented mainly in a non-sequential form.

Results

The condition at operation, in terms of the operating-time, the bleeding seen at operation, and the amount of blood loss, appeared to be the same in both series. The general anaesthetic used for all patients in the trial was supplemented by a local anaesthetic in 14 patients in the chymar group and in 11 patients in the control group.

The main results after operation are summarized in Tables II–IV. In Tables II and IV the figures enclosed within boxes indicate the number of pairs where the assessment was the same for both patients—that is, "tied pairs." The figures in the south-west corner indicate the number of instances where the result with chymar was better than the control, and those in the north-east

TABLE II.—*Comparison of Immediate Post-operative Oedema (Up to 48 Hours) Between Pairs of Patients*

Time Observed after Operation	Degree of Oedema in Chymar Group	Degree of Oedema in Control Group: Marked	Usual	Less	None	Total No. of Pairs
24 hours	Marked	1	2	1	1	5
	Usual	1	1	4	1	7
	Less	—	3	5	1	9
	None	1	1	3	2	7
	Total No. of pairs	3	7	13	5	28
48 hours	Marked	—	2	1	1	4
	Usual	1	—	5	3	9
	Less	—	1	1	3	5
	None	—	7	—	3	10
	Total No. of pairs	1	10	7	10	28

TABLE III.—*Comparison of Late Post-operative Oedema (More than 48 Hours) Between Pairs of Patients*

Oedema Observed in Chymar Group	Oedema Observed in Control Group: Present	Not Present	Not Stated	Total No. of Pairs
Present	6	7	1	14
Not present	6	4	1	11
,, stated	2	—	1	3
Total No. of pairs	14	11	3	28

*Now Lecturer in Experimental Plastic Surgery, Postgraduate Medical School, Hammersmith.

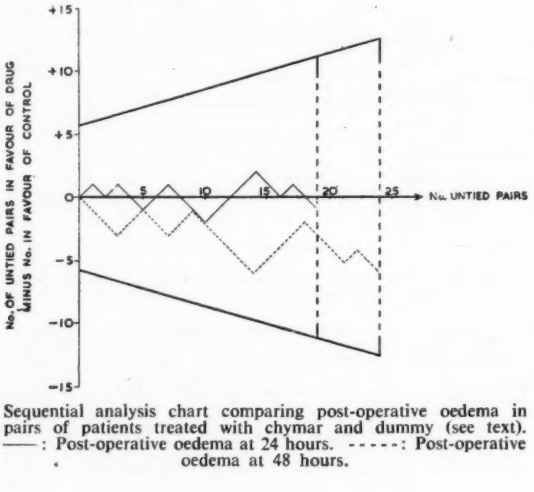
TABLE IV.—*Comparison of Post-operative Bruising Between Pairs of Patients*

Time Observed after Operation	Degree of Bruising in Chymar Group	Degree of Bruising in Control Group					Total No. of Pairs
		Marked	Usual	Less	None	Indefinite or Not Stated	
48 hours	Marked ..	—	3	1	2	—	6
	Usual ..	1	—	2	4	—	7
	Less ..	—	1	2	2	—	5
	None ..	1	5	2	2	—	10
	Indefinite or not stated ..	—	—	—	—	—	—
	Total No. of pairs	2	9	7	10	—	28
7 days	Marked ..	—	—	—	2	—	2
	Usual ..	1	—	2	6	2	11
	Less ..	—	—	—	—	1	1
	None ..	—	5	2	1	1	9
	Indefinite or not stated	1	1	—	2	1	5
	Total No. of pairs	2	6	4	11	5	28

corner the number of instances where chymar was worse than the control. It will be seen that there were virtually no differences between the chymar group and the control group relative to post-operative oedema and bruising. The two groups were compared further for post-operative oozing, wound infection, healing-time, subjective and objective reactions, and local pain, but no differences were found that could not easily have arisen by chance (single tail test with $P=0.05$).

Further examination of the results along sequential lines confirms the conclusions. A sequential analysis chart for post-operative oedema at 24 and 48 hours is included (see Chart). In this chart a preference for chymar is indicated by extending the line one unit in a "north-easterly" direction and a preference for the blank by one unit in a "south-easterly" direction.

At the beginning of the trial the maximum number of preferences was estimated at 40–45, and a restricted sequential procedure (Armitage, 1957) was chosen accordingly. The boundary lines are drawn in such a way that if the two treatments are equivalent there is a probability of approximately 0.95 that the zigzag path will cross the inner broken boundary line and a probability of approximately 0.05 that it will reach the divergent heavy boundary line. On the other hand, if one treatment is an improvement on the other so that 85% preferences are in its favour, then in the long run the zigzag path will hit the appropriate outer boundary about 95 times out of 100. Clearly there was nothing to choose between chymar and the dummy. Most explicitly, the exact probability of reaching by chance the point observed on the inner boundary or one more extreme is, in the case of comparison, at 24 hours 0.50 and at 48 hours 0.16.



Sequential analysis chart comparing post-operative oedema in pairs of patients treated with chymar and dummy (see text). ——: Post-operative oedema at 24 hours. - - - - -: Post-operative oedema at 48 hours.

The observer was asked to state whether he thought the patient had received chymar or the blank. If there was no difference between the two treatments then one would expect that the observer would be right as often as wrong in his judgment. In fact, as Table V shows, this turned out to be the case.

TABLE V.—*Observer's Opinion on Preparation Used*

		Actual Preparation Given		Total
		Chymar	Dummy	
Observer's opinion	Chymar	13	15	28
	Dummy	15	13	28

These results indicate that chymar, given in the stated dose, has no material effect on the degree or incidence of post-operative oedema or bruising.

Discussion

The isolation of crystalline chymotrypsin and an indication of its properties has been described by Kunitz and Northrop (1935), while Tagnon, Weinglass, and Goodpastor (1945) have studied the proteolysis of fibrinogen and prothrombin (and the associated shock) produced by its intravenous injection. Experimentally, intramuscular chymotrypsin in oil was shown to reduce quantitatively the oedema which follows induced inflammation in mice, rats, and guinea-pigs, and such anti-inflammatory activity was greater than that of trypsin (Miechowski and Ercoli, 1956). Work by Hill and Bastrian (1956) suggested that this anti-inflammatory effect was not mediated by the systemic absorption of enzyme resulting in free protease activity; indeed, the exact mechanism of action has not yet been determined.

Clinically, intramuscular chymotrypsin has been used for ocular conditions, Jenkins (1956) reporting favourably on its beneficial effect in traumatic swelling of the eyelids, inflammation of the uveal tract, hyphema, vitreous and retinal haemorrhage, and in certain secondary inflammations. As a local proteolytic agent it has been used to assist removal of the crystalline lens in cataract, though there would still seem to be some doubt about its value (Hill, 1959; Crawford, 1959; Salmony, 1959).

As a therapeutic agent of wide application chymotrypsin has been hailed by Fullgrabe (1957) as a "remarkable anti-inflammatory agent," since it hastens the absorption of oedema and of blood in the tissues. Moore (1959) was able to state, based on experience of its use in 75 patients, that "chymar will revolutionize some aspects of plastic surgery and must be compared to the introduction of antibiotics."

The dosage used in the present trial was twice that recommended by the manufacturers: it was also twice the dose used by Moore, though his patients received chymotrypsin for four days after operation, whereas in the present series treatment was restricted to two days.

In view of the previous findings, why are the results of the present series of 56 patients so disappointing? There are three possible answers.

Firstly, the assessment of the amount of swelling and bruising after operation in any individual patient is a purely subjective valuation based on experience of the type of operation performed, and for this reason a control series is essential. Because assessment is subjective (and cannot be measured objectively), clinical trials should be of the double-blind type. Only in this way is it possible to eliminate conscious or unconscious bias in the observer when a new preparation beneficial to the patient (and surgery) is being evaluated (Truelove, 1959). In none of the papers quoted was the trial "blind," nor apparently were controls included for comparison.

Secondly, bias may also be introduced through the pre-selection of the cases treated: hence the necessity for randomization at the planning stage. In the published reports selection could have contributed materially towards a favourable impression of the preparation.

Finally, a controlled clinical trial, properly conducted, tests not only the preparation under consideration but also its formulation. Hence, in spite of the favourable *experimental* results with chymotrypsin, the unfavourable *clinical* results with lyophilized chymotrypsin could be explained by the altered formulation of the preparation.

Conclusions and Summary

A double-blind controlled clinical trial was carried out on 56 patients undergoing plastic surgery.

Half the patients received chymar (10,000 units intramuscularly one hour before operation, and on each of the next two days) and half received a dummy preparation.

Chymar appeared to have no effect on the degree or incidence of post-operative oedema or bruising in such patients.

We are grateful to the Armour Pharmaceutical Company, who kindly supplied the ampoules of chymar, dummy preparation, and solvent; to the surgeons who allowed their patients to enter the trial; to Sister Sanderson and Sister Downes, who supervised the administration of the preparations; to Mr. W. Trillwood and the dispensary staff, who allocated the patients and maintained the day-to-day supplies; and to Dr. P. Armitage, of the Statistical Research Unit, for providing additional data on the sequential analysis.

REFERENCES

Armitage, P. (1957). *Biometrika*, **44**, 9.
Crawford, R. A. D. (1959). *Brit. med. J.*, **2**, 503.
Fullgrabe, E. A. (1957). *Ann. N.Y. Acad. Sci.*, **68**, 192.
Hill, D. W. (1959). *Brit. med. J.*, **2**, 365.
Hill, R. G., and Bastian, J. W. (1956). *Fed. Proc.*, **15**, 438.
Jenkins, B. H. (1956). *J. med. Ass. Ga.*, **45**, 431.
Kunitz, M., and Northrop, J. H. (1935). *J. gen. Physiol.*, **18**, 433.
Miechowski, W. L., and Ercoli, N. (1956). *J. Pharmacol. exp. Ther.*, **116**, 43.
Moore, F. T. (1959). *Brit. J. plast. Surg.*, **11**, 335.
Salmony, D. (1959). *Brit. J. Ophthal.*, **43**, 321.
Tagnon, H. J., Weinglass, A. R., and Goodpastor, W. E. (1945). *Amer. J. Physiol.*, **143**, 644.
Truelove, S. C. (1959). In *Medical Surveys and Clinical Trials*, edited by L. J. Witts. Oxford Univ. Press, London.

STRESS INCONTINENCE OF URINE

A SURVEY OF 34 CASES TREATED BY THE MILLIN I SLING OPERATION*

BY

CLIFFORD KENNEDY, M.B., F.R.C.S.Ed. F.R.C.O.G.

Consultant in Obstetrics and Gynaecology, Royal Infirmary, Edinburgh

This communication is a survey of 34 cases treated by the Millin sling operation, which was first described by Millin and Read in 1948. Let me say right at the start that there is little place for this operation unless the patient has undergone a previous attempt to cure the incontinence by the vaginal route. This series of 34 cases would suggest, therefore, that my plastic repair results show a considerable number of failures, so far at least as a cure of incontinence is concerned. That, I hasten to say, is not necessarily so, for in the cases reported I have been partly or wholly responsible for the plastic repair operations on 13 cases only. The other 21 were previously treated, over the years, in all three units of the Edinburgh Royal Infirmary, in neighbouring city hospitals, and some, indeed, much further afield. So the fault, if there be one, in plastic repair operations is fairly general.

It is essential, in the first place, that there should be no confusion between the terms "stress" and "urge" incontinence. With the former there is the unconscious escape of urine on straining, laughing, coughing, sneezing, getting in or out of a car or bus, walking, running, and—because of the action peculiar to the game, bending and throwing, and because of the age-group of the women involved—curling. This leak may amount to a few drops only; on the other hand, a mere cough will project—and this can be demonstrated on the examination couch—an appreciable stream several yards across the room. I have seen this on several occasions. There is no associated history of frequency or dysuria in these cases.

With urge incontinence the picture is entirely different. Here there is a low-grade infection, there is often frequency, and there may be dysuria. The patient has the sudden desire to void urine, and if this cannot be done promptly there is a leakage, of which the woman is fully aware. And so there should be no mistake, on careful questioning, about which condition presents, and yet in the hospital out-patient departments one constantly finds a clinical confusion in the history and a faulty diagnosis as a result.

Incidence.—While Gainey (1943) has estimated that approximately 5% of all adult women suffer some degree of stress incontinence, the figure for the frequency of this symptom in association with utero-vaginal prolapse has been put by Bailey (1954) at 39% in 424 cases and at 50% by Read (1950). In a follow-up of plastic repair operations Stallworthy (cited by Read, 1950) estimated the persistence of this symptom at 16%, and both Kennedy and TeLinde (cited by Read, 1950) at 5%–10%. Millin and Read (1948) agree that this figure increases with time, and Counseller (1943) believes it to be as high at 30%. Bailey (1954) found that in a series of 84 patients who had prolapse and stress incon-

*Paper read to the Edinburgh Obstetrical Society on February 10, 1960.

tinence, only 38.5% were cured of their incontinence by the Manchester operation after two years.

Types of Stress Incontinence

The two main varieties are: (1) congenital; (2) acquired—(*a*) post-partum, (*b*) post-menopausal, and (*c*) post-operative.

Congenital.—This form is extremely rare, though it so happens that I have had several such cases under observation fairly recently.

Acquired.—(*a*) *Post-partum:* This is by far the commonest acquired type, the causal factor being trauma associated with childbirth—the prolonged second stage, the difficult forceps extraction through malposition or disproportion, each playing its part in damaging the bladder-sphincter mechanism. (*b*) *Post-menopausal:* It is not uncommon for a stress incontinence to show for the first time at this stage. Presumably the atrophy which occurs in the musculo-fascial supports is responsible, and this is almost certainly the cause where incontinence troubles the nullipara. It is important, incidentally, to realize that this symptom, though usually associated with urethrocele, cystocele, or prolapse, may occur where no evidence exists of any such lesion. (*c*) *Post-operative:* It is a disconcerting fact that incontinence may present for the first time, fortunately rarely, after a plastic repair operation. Where no incontinence is present it is a great mistake to carry the repair of the cystocele too near the urethra and its immediate surround. No purpose is to be gained by such a procedure, and indeed only harm can be done.

Diagnosis of Stress Incontinence

With a careful history and vaginal examination there is usually little doubt that the condition is one of stress incontinence. There is the typical picture of pelvic-floor laxity with cystocele or urethrocele formation, and when the patient is asked to strain the tell-tale leak is evident. In cases of doubt the urethral elevation test described by Bonney (1942) can be used. Two fingers, one on each side of the midline, are applied with some pressure well up on the anterior vaginal wall. In this way the bladder-neck area is raised, and if there is now effective bladder control on straining the diagnosis is confirmed and the success of raising the bladder base by operation may be estimated. Less often it may not be so easy. The patient may be nulliparous and no laxity is apparent. Here it is important to remember that a basal cystitis may produce an urge incontinence; that neurological lesions—tabes dorsalis, disseminated sclerosis, and cord injury—may be responsible; and that congenital bladder abnormalities, calculi, and tumours may be the primary fault. It is essential in such cases to have a neurological investigation and cystoscopic examination carried out.

The Control Mechanism

Much has been written about this and we still do not know the answer. John C. Ullery (1953), of Philadelphia, wrote: "The first early anatomic treatises dealing with the musculature of the urethra and the vaginal wall were made by Galen in which he described the urinary bladder as being composed of longitudinal, transverse, and oblique fibres with the sphincter in the region of the internal meatus and controlling the escape of urine." Since those days this point of view has been supported and it has been denied. My own belief has always been that the main control, and indeed almost the only control, is at the bladder-neck, and it would seem to be a matter of academic importance only regarding the make-up of this particular mechanism. Testut (1894) has described it as consisting of "circular fibres at the vesical neck." Zangemeister (1908) wrote of the smooth-muscle mass at the internal urethral meatus area consisting of bundles traversing obliquely into the bladder to form the "sphincter trigonalis." Ludinghausen (1939) believed that the sphincter—he called it the lissosphincter—consisted of two horseshoe-shaped loops of muscle at the bladder-neck area—one pulling anteriorly and one posteriorly, so shutting the urethra placed between.

The point I would make is that those writers—and these views are just one or two chosen at random—believe in a bladder-neck sphincter or sphincter-like mechanism. There are, no doubt, what might be called "secondary" sphincters—the pubo-coccygeus muscle (the most medial fibres of the levator ani), the urogenital diaphragm consisting mainly of the sphincter urethrae and deep transverse perineal muscle, and, nearer the surface, the bulbo-cavernosus and ischio-cavernosus muscles. Now it has been shown that if half or even more of the urethra is removed—and with it must obviously go the more intimate connexions from those "secondary" sphincters—the patient can still be continent. What better argument for the bladder-neck "sphincter" being the main and only control?

Cause of Stress Incontinence

Much investigation has been carried out in the last twelve years by radiographic study to show how the bladder empties normally and to explain why sometimes there is stress incontinence. Millin and Read (1948), Muellner (1949), Ball (1950), and Jeffcoate and Roberts (1952a, 1952b) have all described a descent of the bladder-neck or loss of the posterior urethro-vesical angle in women exhibiting this symptom when intra-abdominal pressure is increased. Read went so far as to say that "the degree of descent in most cases varies with the degree of incontinence." With this last opinion I would most strongly disagree. For descent to occur most of us believe there must be weakening of the pubo-cervical fascia and possibly of the pubo-coccygeus muscle. Now if there were this weakening, there would also be cystocele, and so, in the same way, it might be said "the bigger the cystocele the greater the incontinence." But this is not so. Indeed, how often is the reverse true?

It is argued further that this descent is important, not because of the accompanying cystocele, but because this downward and backward movement of the bladder-neck is associated with loss of the posterior urethro-vesical angle and the so-called funnelling of the exit, as happens in normal micturition. I have never subscribed to this idea and Simmons (1955) has denied such changes during micturition, and certainly the post-operative *x*-ray findings in this series support his view. Of nine patients chosen at random to be *x*-rayed, seven had complete control and two had occasional stress leakage. Of the seven, the angle was preserved in five and lost in two during micturition. Of the other two where there was a leak from time to time, the angle was well preserved in both, and so I would say that there is little or nothing in this theory of funnelling and loss of posterior urethro-vesical angle. A patient may be continent with no angle,

and the reverse may hold equally. It is my contention, therefore, that bladder control depends almost entirely on the efficiency of the internal sphincter mechanism situated in the bladder-neck. This efficiency can be upset by stretching or loss of tone resulting from parity, menopausal atrophy, or some general systemic disease. Indeed, it is even possible that no other factor is involved. It may well be as simple as that.

Prophylactic Treatment

Prophylaxis is all-important and consists in the most careful supervision and management of labour. Obviously the second stage and actual delivery are of greatest significance. In a primigravida, the second stage should not be allowed to exceed three hours—indeed, it may be cut short before that under certain circumstances —and the bladder must always be kept empty. Once the cervix is fully dilated, the bladder is displaced forward by descent of the foetal head, and it is then that the internal sphincter mechanism may be damaged. This is especially likely to occur if the musculature is already over-stretched. A delivery associated by more than average traction with resulting excessive trauma will also play its full part in stress aetiology. And so, therefore, correction of any malposition and adequate episiotomy, in those cases where there is obvious difficulty, are essential before an attempt at delivery is made.

For the puerperal patient, where there is often a slight and fortunately temporary tendency to incontinence, appropriate exercises to tone up the perineal musculature may be practised, sometimes with complete benefit. For this purpose the perineometer of Kegel (1948) may be used. Here the levator ani muscles are contracted, and a dial attached to this instrument, which has been placed in the vagina, registers the force of the contraction. The aim of the patient is to increase this force and so strengthen her pelvic musculature.

This may have been tried and proved unsuccessful, or, on the other hand, the incontinence may be marked from the beginning. In such cases some form of plastic vaginal operation is called for, particularly where utero-vaginal prolapse is also present and the patient is finished with child-bearing. Let it be said again that an attempt at cure should almost always be made by the vaginal route in the first place.

It is quite impossible, where the previous repair operations have been done by others, to find out the exact technique employed, but it is fair to surmise that three main methods were used: (1) the Manchester operation; (2) anterior and posterior repair without amputation of the cervix; and (3) anterior repair only in younger women where, from the viewpoint of future child-bearing, it is inadvisable to tighten the pelvic floor unduly.

Of these three procedures there can be little doubt that the Manchester operation, or our own version of it, is the most popular. But is this enough where incontinence is present? As already stated, Bailey (1954) found a cure in only 38.5% two years after this treatment. And therefore some modification is necessary if this procedure is to be effective. So it is that we find special techniques devised by Kelly *et al.* (1928), Kennedy (1941), Pacey (1949), and TeLinde (1951), to mention but a few. Of these, the "Kelly stitch," as it is commonly called, is possibly most practised. It is a simple procedure and has proved successful, according to some writers, in 85% of cases so treated. Here the bladder-neck area, after being freed from the vaginal wall, is raised and supported by several mattress sutures. The suture material used depends on the operator, but Kelly used fine silk. TeLinde's operation was a little more extensive in that mattress sutures were employed along the whole length of the urethra in addition to those placed in relation to the bladder-neck.

Kennedy and Pacey went further and included not only plication of the pubo-cervical fascia but approximation of the levator ani muscles, where they were attached to the vaginal walls, with silver wire, or approximation of the pubo-coccygeus muscles with interrupted chromic-catgut sutures. Most of us have tried one or other of those manœuvres, and no doubt we are quite smug about our results. But just when we are most smug, along comes a patient and her story is humbling, for she is still incontinent. Now, it is fair to say that the indifferent surgeon has his successes; the human frame is tough and is often responsive to what amounts to suggestion only, for in many cases the technique employed is likely to be quite inadequate. What is equally true to say is that the good surgeon occasionally has his failures. And this may not be the fault of the surgeon, for there is no doubt that much must depend on the patient's own tissues. Bad material, no matter how good the tailor, falls out of shape quite soon, and exactly the same rule applies in the case of a plastic repair. And so, therefore, for one reason or another there are patients where one or more vaginal operations have failed to cure the incontinence. The prolapse has gone completely, the pelvic floor and vaginal walls are tight, but the patient is still uncomfortably wet on exertion. Further operative treatment is essential, and for this type of case many operative procedures have been devised.

Treatment of Stress Incontinence after Plastic Repair Operations

Those procedures may be divided into the following groups: (1) fascial slings placed under the urethra or bladder-neck area, (2) fixation of the bladder and urethra to the symphysis pubis, and (3) separation of the bladder and urethra from the symphysis pubis.

Other operations have been described, one of the more recent being advocated by Louros (1959). His technique is based on the belief that incontinence depends on abnormal curving of the urethra and sagging of the bladder-neck. Ventrofixation is first performed to correct any associated retroversion. The vesico-uterine fold, unopened, is raised from the depth of the vesico-uterine space and sutured to the posterior uterine wall to remedy retroflexion. As a result of this the bladder fundus is drawn backward, the bladder-neck is elevated, and the urethra is straightened. Any laxity of the vaginal wall is dealt with, before the laparotomy, by a plastic repair. The success of this procedure is given as 93%.

1. In the first group the Aldridge (1942) operation, later modified by Studdiford (1946), consists in carrying out a Kennedy plastic repair and in bringing down through the retropubic space, lateral to the bladder and under the urethra, two transverse fascial strips of external oblique aponeurosis. A sling is formed in this way. This operation has both an abdominal and a vaginal approach, and it was argued that the latter might predispose to an infection. A cure rate of 82% was reported after an interval of two years. Millin and Read (1948) described a sling operation,

the Millin I operation, where through a curved transverse lower abdominal incision the retropubic space is opened into. Two strips of aponeurotic fascia, one pedicled on the right and the other on the left at the level of the anterior superior spines, are passed through the rectus muscles and underneath the bladder-neck. The two strips are stitched to one another with nylon and the degree of elevation of the bladder-neck can be very finely judged by this method. In 1950, using a 20-cm. strip of fascia lata, Millin adopted a further technique, the Millin II procedure, which might almost be described as the Aldridge operation in reverse. Here the fascial strip is placed under the urethra and the ends are forced up behind the pubis, rather than brought down, and fixed to the rectus sheath through an abdominal incision. Again there was in this method the double approach and the same chance of infection.

2. Of operations designed to fix the bladder and urethra to the posterior surface of the pubis, the Marshall, Marchetti, and Krantz (1949) is the most popular in this country to-day. With an abdominal approach the urethra and bladder-neck are fixed to the periosteum by a series of chromic-catgut sutures. The bladder is also sutured to the posterior aspect of the rectus muscles. Here the cure rate has been placed around 74% and the improved rate at 92%.

3. Mulvany (1951) described how, through a transverse suprapubic incision, he freed digitally the bladder-neck and urethra from the pubic arch. His belief was that the bladder-neck so freed was able to contract and retract more efficiently. A cure rate of 88% was reported after four years. It has been said by Stabler (1952) and others that this procedure is effective not so much because adhesions are broken down, but rather because more form as a result of what has been done. In other words, this is merely another method of raising and fixing the bladder to the pubis.

The Millin I operation has not become tremendously popular, for two simple reasons: it is technically, on occasion, very difficult to place the fascial strips under the bladder-neck and there is a high incidence rate of injury to the bladder or urethra. I would not agree, however, that it is difficult to estimate the tension of the sling. On the contrary, I would claim that it is possible to do just this with great accuracy, and the ease with which this is done constitutes one of the main advantages of the technique. The technical difficulty arises from the dense scar tissue and adhesion formation between urethra and vaginal wall, the result of previous plastic repairs, and it is through this tissue that a tunnel has to be forced for the strips. I have had the Millin forceps modified—it has been lengthened by 2 to 3 in. (5 to 7.5 cm.) and the points have been sharpened. Placing the strips has become easier, less force is necessary, and injury may lessen. But, if injury should occur and there is suprapubic leakage of urine, continuous bladder drainage by a self-retaining catheter and drainage of the retropubic space should ensure healing of the bladder within ten days or so, sometimes sooner. No sling in this series has had to be undone, or divided, and on no occasion has the sling, through being too tight, cut through the urethra.

Analysis of the Series

And now, very briefly, a word or two regarding several points which were analysed in this present series of 34 cases.

Table I shows a lack of relationship between the duration of symptoms and the degree of parity. The four longest periods of incontinence, from 20 to 30 years in fact, were in no case associated with a parity greater than two. And so it can be said that the mother of the large family is not necessarily the one to have a long-standing symptom history. In three cases the duration of incontinence in the case record was stated as "many years," and in these a period of 10 years was allowed. The average duration of the incontinence was 8.7 years.

TABLE I.—*Duration of Symptom in Relation to Parity*

Duration	Parity
30 years	2
25 ,,	2
20 ,,	1
20 ,,	0

TABLE II.—*Influence of Parity*

Parity	0	1	2	3	4	5	6	7	8	9	10	11
No.	6	5	11	2	5	2	0	1	0	0	1	1

Parity varied from 0 to 11 (Table II). It is significant that the biggest group of cases, 11 in number, are associated with a parity of 2. The present-day tendency to the small family may to some extent explain this finding, but it is not the whole explanation. There are only two cases in the para-3 and five cases in the para-4 groups. Incontinence was present in six nulliparae. The average parity was 2.6.

TABLE III.—*Age Incidence*

Age-group	21–30	31–40	41–50	51–60	61–70	71–80
No.	0	2	16	9	5	2

Table III shows that the age-groups most commonly involved were those of 41–50 and 51–60. This is exactly as it should be, in that the bladder-sphincter mechanism, already weakened by the trauma of labour, is further weakened by menopausal atrophy.

There were six nulliparae in the series, three married and three unmarried—an operation rate in this type of case of 17.6%. Three of the six had had a previous plastic repair and a fourth developed incontinence after extensive cauterization of a urethral caruncle some years before.

Twenty-five patients had had one previous plastic repair, four had two attempts at vaginal cure, and two patients had three. That makes a total of 31 cases. The remaining three had had no previous repair, and in those a sling operation was the first method of treatment—a frequency rate of 8.8%.

Where several vaginal operations had been performed the longest interval between the first of those and the subsequent sling was 32 years. Where only a single repair had been carried out the longest interval was 20 years and the shortest six months. Various figures have been quoted regarding the cure rate of stress incontinence by vaginal repair, and, though it is true that most failures show up after several years, some are obvious when the patient pays her post-operative reporting visit in a month or two.

In nulliparous patients particularly, and where no obvious laxity was apparent, it was the custom to have a cystoscopic examination carried out. This was done in eight patients, and in only one was abnormality found in the form of a basal cystitis.

The average stay in hospital after operation was 26.5 days, the shortest period being 15 and the longest 43.

Eighteen cases showed infection of the urinary tract, and the same number experienced bladder trauma at

operation—a percentage rate of 52.9. This, as has been said already, is one of the reasons why this particular method is not so popular as it might be.

Five cases showed wound infection. The reason for a rather prolonged convalescent period in certain patients is thus apparent.

In 1950 there were two deaths, and neither was directly related to the particular type of operation employed. The first was due to a massive pulmonary embolism on the seventeenth day, when all seemed well. The other occurred two days after operation. Here necropsy showed a liver necrosis, and it is fair to assume that this was not unrelated to the bromethol anaesthesia which had been employed.

And now for the really important point—the result of the operation. Regarding the term "complete control" there can be no dubiety. "Almost complete control" means simply a very occasional and slight leak when the bladder is full and the patient is making some special physical effort.

I think it is proper to include both groups under the term "cure"—a rate of 87.5%. This compares very favourably with the results of other types of sling operation. Two cases showed improvement and there were two absolute failures.

Conclusions

To conclude, I would say just this. In the parous patient with laxity of the vaginal wall and stress incontinence, an attempt at cure should always be made in the first place by a vaginal plastic repair operation. If this has been done and a stress incontinence still exists without laxity, then there is a place, and a most important place, for some form of sling operation. I would go further. There is also indication, on occasion, for this latter operation in the nullipara; for here, too, there is often no apparent laxity and nothing can be done by a routine repair procedure. Such cases, however, should always have the bladder and nervous system investigated before operation is undertaken.

The analysis of this series was carried out simply because I wished to ascertain just where the Millin I sling operation stood, so far as the results were concerned, with operations of a similar type. There can be no doubt that the comparison is very favourable. And so, though this operation may sometimes be technically difficult, though there is a high percentage of temporary bladder trauma, and though the immediate post-operative nursing is exacting and the convalescence a little prolonged, I would suggest that this procedure might be practised more often with advantage.

Summary

In this survey the clinical picture in "urge" and "stress" incontinence is described. The incidence of stress incontinence in association with utero-vaginal prolapse and the cure rate of this symptom by the standard plastic repair operations are discussed. Reference is also made to the diagnosis and differential diagnosis of stress incontinence.

In relation to the control mechanism of the bladder, the anatomical views of certain writers are quoted. It is thought that the loss of the posterior urethro-vesical angle plays little or no part in aetiology—this is supported by *x*-ray findings—and that the sole cause lies in weakening of the sphincter mechanism in the bladder-neck area.

The various plastic procedures for treating stress incontinence are described, and where those fail the more popular types of sling and fixation operation, which must then be considered, are mentioned. The cure rate of the different operations is contrasted.

Finally, the results of 34 cases treated by the Millin I operation are fully discussed. Thirty-one patients had had one or more previous plastic repair procedures carried out; in three the Millin operation was the first method of treatment. The cure rate in this series is 87.5%, a figure which compares more than favourably with comparable methods of treatment.

My thanks go to Miss West and to Sister Isdale for helping with the cystograms, and to Sister Robertson and Sister Michie, who helped with the nursing of the patients and made a very real contribution to any success there may have been.

REFERENCES

Aldridge, A. H. (1942). *Amer. J. Obstet. Gynec.*, **44**, 398.
Bailey, K. V. (1954). *J. Obstet. Gynaec. Brit. Emp.*, **61**, 291.
Ball, T. L. (1950). *Amer. J. Obstet. Gynec.*, **59**, 1243.
Bonney, V. (1942). *A Textbook of Gynaecological Surgery*, 4th ed. Cassell, London.
Counseller, V. S. (1943). *Amer. J. Obstet. Gynec.*, **45**, 479.
Gainey, H. L. (1943). Ibid., **45**, 457.
Galen. Cited in T. Lauth's *Histoire de L'Anatomie*. Strasbourg, 1815.
Jeffcoate, T. N. A., and Roberts, H. (1952a). Ibid., **64**, 732.
—— —— (1952b). *J. Obstet. Gynaec. Brit. Emp.*, **59**, 685.
Kegel, A. H. (1948). *Amer. J. Obstet. Gynec.*, **56**, 238.
Kelly, H. A., and collaborators (1928). *Gynecology*. Appleton, New York.
Kennedy, W. T. (1941). *Amer. J. Obstet. Gynec.*, **41**, 16.
Louros, N. C. (1959). *Zbl. Gynäk.*, **81**, 225.
Ludinghausen, M. (1939). *Gynecological Operations and their Topographic Anatomy*. DeBour.
Marshall, V. F., Marchetti, A. A., and Krantz, K. E. (1949). *Surg. Gynec. Obstet.*, **88**, 509.
Millin, T. (1950). *Proc. roy. Soc. Med.*, **43**, 258.
—— and Read, C. D. (1948). *Postgrad. med. J.*, **24**, 51.
Muellner, S. R. (1949). *Surg. Gynec. Obstet.*, **88**, 237.
Mulvany, J. H. (1951). *J. Obstet. Gynaec. Brit. Emp.*, **58**, 449.
Pacey, K. (1949). Ibid., **56**, 1.
Read, C. D. (1950). In J. V. Meigs and S. Sturgis's *Progress in Gynecology*, 2nd ed., p. 690. Heinemann, London.
Simmons, C. A. (1955). Cited in T. L. T. Lewis's *Progress in Clinical Obstetrics and Gynaecology*, p. 362. Churchill, London.
Stabler, F. (1952). *J. Obstet. Gynaec. Brit. Emp.*, **59**, 708.
Studdiford, W. E. (1946). *Surg. Gynec. Obstet.*, **83**, 742.
TeLinde, R. (1951). *Operative Gynecology*. Lippincott, Philadelphia.
Testut, L. (1894). *Traité d'Anatomie Humaine*, 2nd ed. Doin, Paris.
Ullery, J. C. (1953). *Stress Incontinence in the Female*. Grune and Stratton, New York.
Zangemeister (1908). *Z. gynäk. Urol.*, **1**, 1, 79.

Dr. R. K. CALLOW and Miss NORAH C. JOHNSTON, of the National Institute for Medical Research, Mill Hill, have succeeded in identifying and synthesizing "queen substance," the hitherto unknown chemical substance which controls reproduction in honeybee colonies. (It is not the substance known as royal jelly.) Its constitution is that of 9-oxodec-2-enoic acid, $CH_3CO.[CH_2]_5CH:CH.COOH$. In recent years it has been demonstrated that the queen bee produces a substance in her mandibular glands which her worker bees obtain in the process of caring for her. This substance becomes distributed throughout the colony, and prevents the workers from raising any new queens. It also prevents the development of the ovaries of worker bees. It is possible that it may have some allied effect in other animals, including man, and other pharmacological properties. (*Bee World*, Bee Research Association, June, 1960.)

BEPHENIUM HYDROXYNAPHTHOATE IN TREATMENT OF ASCARIASIS

BY

GLADYS JAYEWARDENE, Ph.D., D.T.M.&H.

M. M. ISMAIL, M.B., B.S.

AND

Y. WIJAYARATNAM

From the Medical Research Institute, Colombo, Ceylon

In the course of the clinical trials with bephenium compounds against hookwoorm in Ceylon (Goodwin, Jayewardene, and Standen, 1958) it was found that concurrent infections with roundworm were also cleared in the majority of cases treated. Early in 1959 bephenium hydroxynaphthoate was used, in divided doses, over a period of days, to test its efficacy against whipworm infections. The action of the drug against roundworm was again observed; a large number of children passed roundworms on the first day of treatment, some within half an hour of taking the drug. As the drug was employed in a much smaller dosage than for hookworm infections its action against roundworm appeared to be considerable.

In view of this it was decided to determine the minimum effective single dose for mass anti-ascariasis treatment, and the minimum dose required for total clearance of infection.

Material and Methods

In the hookworm trials it was established that the effective dose of the bephenium compounds was the same for adults and children. Children were therefore selected for this trial as they were more likely to have infections with roundworm. At the start children residing in state homes and orphanages were selected as they were in organized groups that could be supervised. Later, children from homes in poor sanitary conditions were treated. These homes, however, were in groups which were conveniently placed for mass treatment. Subsequently a few adults, mainly patients from the General Hospital, Colombo, were included in the series.

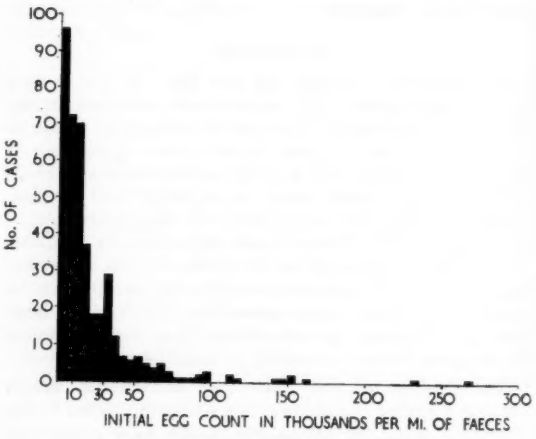
All subjects were taken at random and divided into groups. The only precaution taken was to see that each group had roughly the same age distribution.

Faecal samples were collected in small cartons. These were first examined by the direct saline smear method. Those found positive had an ova count by a modified Stoll method (Stoll and Hausheer, 1926). Follow-up examinations were made on the fourth day after treatment. In a few instances the follow-up was delayed, but in none did the delay exceed two weeks. The follow-up samples were examined by the direct saline smear method. If found negative they were then examined after concentration, using the M.I.F. technique (Blagg, Schleegel, Mansour, and Khalaf, 1955). The positive samples had an ova count done in duplicate.

In assessing the results of treatment, all follow-up specimens which were negative even after concentration were regarded as being 100% cleared of infection. Those negative on direct smear but positive on concentration were estimated to have fewer than 200 eggs per ml. of faeces, and were also grouped as being 100% cleared. In those positive on direct smear the percentage reduction on the original egg count was determined, and is referred to as "percentage clearance."

Bephenium hydroxynaphthoate ("alcopar") was kindly supplied by Messrs. Burroughs Wellcome Ltd. Different preparations were tried on various groups to determine the best method of masking the bitter taste of the drug. Some groups had plain granules suspended in water, while others had the drug in a 3.5% sugar solution flavoured with essence of lemon. A peppermint-flavoured suspension and chocolate-coated granules were used on other groups. These two preparations were supplied as such by the firm. (In practice, we found a sweet, such as a fruit-drop, very useful for tempting small children to take the drug.)

The drug was given at different times of the day. Some had it first thing in the morning on an empty stomach, the morning meal being taken about one to one and a half hours later. Others had the drug last thing at night, about three hours after their last meal. When two doses of the drug were given on the same day, the second dose was given at about 3 p.m., three to four hours after the midday meal. In no case was a purge employed.



Weight of infection before treatment.

Results

In all, 396 subjects were treated. The dose employed varied from group to group. Infection in the children varied from light to very heavy, the highest count being 265,000 eggs per ml. of faeces. The Chart shows the distribution of infection. Table I shows the percentage clearance of eggs in relation to the dose employed.

When a dose of 0.625 g. was used, only 35.7% of cases (28 treated) showed over 80% clearance. More

TABLE I.—*Dose and Percentage Clearance in Egg Count*

Dose (g. of Bephenium Base)*		No. Treated	Clearance 80% and Over	
			No.	%
0·625		28	10	35·7
1·0		48	27	56·2
1·25		55	39	70·9
1·66		59	38	64·4
2·0		47	36	76·6
2·5	with syrup, etc.	37	31	83·8
		56	45	80·4
	chocolate-coated	19	14	73·7
2×1·25		54	48	88·9
2×1·66		49	46	94·0

* Dose throughout is in terms of bephenium base. Corresponding dose in terms of bephenium hydroxynaphthoate granules is double this figure.

TABLE II.—*Distribution of Cases with More than 80% Clearance in Relation to Initial Egg Count and Dose*

Initial Egg Count in 1,000's	Dose (g.)																	
	0·625		1·0		1·25		1·66		2·0		2·5*		2·5†		2×1·25		2×1·66	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
< 5	6	50	13	54	11	46	13	69	20	67	11	91	7	43	7	71	10	90
5<10	4	50	9	67	9	78	12	42	10	70	7	57	2	50	11	82	10	90
10<20	10	40	6	50	14	71	16	69	8	100	9	90	7	100	13	92	11	91
20<30	3	0	3	0	5	80	5	60	4	100	4	100	3	100	8	100	3	100
30<40	—	—	7	71	7	71	5	60	2	100	3	100	—	—	5	80	9	100
40 and over	5	20	10	50	9	89	8	87	3	100	3	66	—	—	10	100	6	100
Total ..	28	36	48	56	55	71	59	64	47	77	37	84	19	74	54	89	49	94

* Granules given with syrup or water. † Chocolate-coated granules given with water.

children were not treated with this dose as it appeared inadequate.

With a dose of 1 g. a larger number of cases had 80% clearance, but there were many failures in persons with initial counts of 20,000 or more eggs per ml. of faeces. When a dose of 1.25 g. was employed, the clearance obtained in cases with initial counts of 20,000 or more eggs per ml., was dramatic. The higher the count the more effective was the clearance. 71% of cases treated had more than 80% clearance. The majority of failures in this group were among those with counts of fewer than 20,000 eggs per ml. of faeces.

The results obtained with 1.66 g. appeared to be less satisfactory than those obtained with 1.25 g., but the difference was not statistically significant. Generally, however, Table I shows that with increasing dosage an increase in the number with 80% clearance of infection is to be expected. When two doses of 1.25 g. or two doses of 1.66 g. were given on the same day, 80% of clearance was obtained in 90% and 94% of subjects respectively.

Table II shows the percentage clearance obtained with different doses in relation to the initial egg count. It was mentioned earlier that with doses of 1.25 g. or more the majority of cases with counts of 20,000 or more eggs per ml. had over 80% clearance of their infection. This is clearly seen in Table II. This group, however, had two cases with egg counts between 40,000 and 50,000. One had over 80% clearance, the other had 68.5% clearance. In the same group, of those with low counts of fewer than 5,000 eggs (11 cases), only 46% had 80% clearance. But at all higher infection levels, 70% or more had over 80% clearance of infection. With lower doses less than half the subjects had 80% clearance of infection, whatever the original level of infection.

Table III shows the incidence of vomiting in relation to the dose. It will be seen that the incidence of vomiting increased with the rise in the dose from 0.625 g. to 1.25 g. However, the two smallest doses were ineffective for roundworm, and therefore the lower incidence of vomiting with these can be disregarded for practical purposes. With doses above 1.25 g. the incidence of vomiting was not significantly different except for the dose of 2.5 g. of chocolate-coated granules and that of 2×1.66 g., where the vomiting was significantly less. The former result is probably due to the chocolate being an effective mask for bitterness. The latter result cannot be accounted for so easily. It may be due to several other factors (see below).

TABLE III.—*Vomiting in Relation to Dose*

Dose (g.)	No. Treated	Vomiting	
		No.	%
0·625	28	3	10·7
1·0	48	8	16·7
1·25	55	13	23·6
1·66	59	17	28·8
2·0	47	17	36·2
2·5 with syrup, etc.	37	12	32·4
2·5 chocolate coated	19	1	5·3
2×1·25 peppermint flavoured	28	16	38·8
2×1·25 lemon flavoured ..	26	5	
	54	21	
2×1·66	49	8	16·3
Total	396	100	25·0

In relation to age, the incidence of vomiting was significantly greater in children under 4 years old in all groups except those receiving the ineffective doses of 0.625 g. and 1 g. Of 325 children over 4 years, 70 vomited and of 71 children under 4 years 29 vomited. (The chocolate-coated granules were bulky and were not given to children under 4 years of age.)

The time of administration did not have an observable effect on the results obtained, except that vomiting was more likely to occur if a meal was taken immediately after or before the drug. When two doses of the drug were given on the same day the incidence of vomiting was not significantly different between those having the midday meal three hours before the second dose and those having it four hours before.

The results show that 1.25 g. can be regarded as the minimum effective dose, because with this dose 86% of the children passed worms, 71% had over 80% clearance, and practically all those with initial counts of more than 20,000 eggs had also over 80% clearance.

Discussion

In countries like Ceylon, where there is no immediate prospect of improving prevailing insanitary conditions or cleaning up seeded soils, the only means of preventing children from being overburdened with ascarides is by regular treatment. For example, in our previous hookworm and whipworm series, almost all patients who had incidentally been cleared of roundworm infection were subsequently found to have unfertilized roundworm ova in their stools at the end of four weeks. We also had the opportunity of examining over 100 children six months to one year after they had been treated with full doses of piperazine citrate (" antepar "). (Most of them had had bephenium compounds as well.) Practically all the children were found to be infected again to about their original level. This could only mean that reinfection is continually occurring, as judged by the known resistance and longevity of the roundworm egg. In these circumstances the value of administering massive doses of anthelmintics for complete clearance of infection is of questionable value. This is particularly so with regard to mild infections.

The dose of bephenium hydroxynaphthoate recommended by us is small, is acceptable to all ages, causes very little vomiting, and is effective. If a more thorough clearance is sought, two such doses should more than suffice, given either on the same day or on two successive days.

In the treatment of hookworm infection, where the worms are closely attached to the bowel wall and where there must be an empty bowel to ensure close contact between worm and drug, it is essential that the drug be given first thing in the morning. In roundworm infection also, the best time for administering the drug is in the morning, but it may also be given last thing at night after an early dinner. Where two doses are given on the same day, it is best to give the midday meal early, at about 11 a.m., and the second dose about four hours later. Here it must be noted that when a meal is taken shortly before or soon after the drug there is a greater tendency to vomit.

In our experience the best preparation was the freshly prepared suspension in lemon-flavoured syrup. Most children accepted this, and some of the 2-year-olds even sipped it at leisure. (The other preparations are discussed in relation to the incidence of vomiting.)

In treatment of ascariasis with bephenium hydroxynaphthoate the daily programme of the school child is upset only by the passage of worms. Worms are passed from within half an hour of taking the drug to three days later. They are generally alive when passed, but by about 24 hours the majority are dead and the rest only feebly active. A few children stated that they vomited coils of small worms. We did not have an opportunity of examining these, but they were presumably developing roundworms en route in the stomach or the upper reaches of the small bowel.

In considering the failures of treatment when presumably adequate doses (1.25 g.) were employed, it was observed that the majority were in those with low initial egg counts. This was also observed in the trials with bephenium compounds against hookworm (Goodwin *et al.*, 1958). With low egg counts a difference of a count of one egg is reflected 100 to 200 times in the final count, so that an appreciable error either way is possible; but this is the only practical way of assessment in large-scale work. Wang Cheng-Yi (1959) has suggested a method of culturing the stool whereby the eggs are allowed to hatch and all the larvae are counted. He states that this method is of particular value in avoiding the error that is likely to arise in low counts, that "in counts of $> 5{,}000$/ml. the mean value of ova as determined by the two methods (Stoll's and culture) were about the same . . . but as the number of ova decreased $< 5{,}000$/ml. then the figures obtained by Stoll's technique and the present method differed quite a bit." He concludes that "when the infestation is heavy the culture method is as good as Stoll's, but when the infestation is light the culture method is much better than Stoll's."

This error in the low counts may therefore be the cause of our apparent failures. It also appears that a few isolated worms are more difficult to eliminate than those which presumably lie massed together. For some reason the drug does not get at them. This possibility also may have accounted for failures in the hookworm series, where those with low counts showed apparently less response to treatment (Goodwin *et al.*, 1958). This was our observation in the present series also. When a dose of 1 g. was used our first real failures in the high counts occurred. The dose seems to be insufficient to deal with worms even when lying massed together. It therefore confirmed our views that 1.25 g. is the minimum effective dose, as there was a dramatic response to treatment with it.

The only disagreeable side-effect of the drug is vomiting, and that probably owing to its bitter taste. The drug also tends to "repeat."

Most children did not seem to be affected by the worm load itself. They did not feel unwell and so did not welcome the idea of a dose of medicine. In such children and adults the vomiting that occurs is probably largely psychological. For example, we noticed that when one member of a household vomited several others did so soon after; and in well-disciplined groups of children, as in some institutions, vomiting was much less than in others. Again, in the case of hospital in-patients who accepted the drug as part of a normal routine, vomiting was at a minimum.

The incidence of vomiting was highest in those taking the drug as a suspension in water, and much less in those taking it as a freshly prepared suspension in lemon-flavoured syrup. The peppermint-flavoured suspension, when fresh, compared very favourably with that in lemon-flavoured syrup. But after storage for a few weeks it caused a considerable amount of vomiting, though the action of the drug itself was unchanged. This is revealed in Table III. The incidence of vomiting was found to be significantly higher in the peppermint group. The chocolate-coated granules were the best preparation because they caused vomiting in only one out of 19 persons treated. However, their bulk is a disadvantage, for the children tend to swallow the liquid and chew the granules, thus defeating the purpose of the chocolate coating. It is therefore not an acceptable form for the lower age-groups, where the chances of vomiting are greater. It was also observed that in comparable groups taking the drug in lemon-flavoured syrup, almost 100% of the children passed worms, whereas in the group getting chocolate-coated granules, only 9 of the 19 did so. With regard to clearance the results were not significantly different between the two groups, though higher in the group taking the lemon syrup.

The incidence of vomiting is not related to the initial weight of infection. For example, some children with very heavy infections (265,000 eggs per ml.) did not vomit.

We did not observe any laxative effect of the drug, though in children who passed worms there was a frequent desire to pass a stool. This is probably due to the underlying movement of worms. The feeling subsides with the evacuation of worms. We were able to observe this effect better in some other children (not in this series) who were given 1.25 g. of bephenium hydroxynaphthoate twice daily over a period of seven days. Some of them stated that they had two or three "stools" on the first day of treatment, but the "stool" consisted mainly of worms.

We had one case of "shock" (probably from a fall of intra-abdominal pressure) in a 2½-year-old girl with an initial count of 50,000 eggs per ml. of stool. She was not underweight and did not appear undernourished apart from having a somewhat distended abdomen. Bephenium hydroxynaphthoate, 1.25 g., was given at 6.30 a.m., and when we arrived to give her the second dose at 3.30 p.m. we were told that she had passed eight

worms and that she appeared to want to pass a stool all the time. She is said to have passed several coils of worms on the morning of the second day, and by noon appeared to be somewhat listless and cold. She was admitted to hospital for observation and was given a rectal washout and glucose by mouth. She was discharged the same evening and was quite comfortable when seen later that night. She passed a large coil of worms next morning as well.

It was subsequently disclosed that the child had been given a dose of ½-oz. (15 g.) of piperazine citrate two days earlier, but had not passed worms. The parents had not disclosed this to us as they were anxious to have her treated again because she was in the habit of eating plaster off the wall, which they attributed to worm infection. The symptoms that developed were probably caused by a sudden release of intra-abdominal pressure after evacuation of a large number of worms. The distension that followed was probably due to the loss of tone in a gut that had been chronically distended by large masses of worms. We had earlier had this eventuality in mind in not treating under field conditions another 2½-year-old child with an egg count of 199,000, but did not expect it in this particular instance. The possibility of this eventuality should be borne in mind when any child passes large numbers of worms after anthelmintic treatment. The dose could not have been too high, for a younger sister, 1½ years old, had the same dose and was unaffected. The child has since had an improved appetite and her general health is reported to be much better.

We had two sisters, aged 8 and 2½ years, who developed wheezing 36 hours after receiving bephenium hydroxynaphthoate. They had 1.25 g. twice on the same day and had passed 25 and 30 worms respectively. They had no previous history of asthma. The elder girl showed a fair amount of distress when seen by us 48 hours after treatment. They both responded well to an injection of aminophylline, were observed for a period of six hours, and subsequently were quite well. Several doctors in charge of out-patient dispensaries have informed us that wheezing and transient fever are often seen in children treated with piperazine citrate for ascariasis. In our experience these were the only allergic manifestations in over 400 children treated with varying doses of bephenium hydroxynaphthoate.

Vague abdominal pain was sometimes complained of by a few children, but in none was it severe enough to cause anxiety.

Summary

Different preparations of bephenium hydroxynaphthoate ("alcopar") in varying doses were given to groups of children, to determine the minimum effective dose for treating ascariasis.

1.25 g. was found to be the minimum dose with optimum results.

The best preparation was a freshly prepared suspension in lemon-flavoured syrup (3.5%).

Vomiting was the only disagreeable side-effect directly attributable to the drug. It was significantly more in children under 4 years of age.

The small dose recommended for treatment of ascariasis could be safely given to any age-group without causing anxiety.

Our thanks are due to Dr. P. G. Somasundaram, who did the statistical analysis of our results, and to Dr. D. B. Gunasekara, who made many valuable suggestions in the course of our work.

REFERENCES

Blagg, W., Schloegel, E. L., Mansour, N. S., and Khalaf, G. I. (1955). *Amer. J. trop. Med. Hyg.*, **4**, 23.
Goodwin, L. G., Jayewardene, L. G., and Standen, O. D. (1958). *Brit. med. J.*, **2**, 1572.
Stoll, N. R., and Hausheer, W. C. (1926). *Amer. J. Hyg.*, **6**, March Suppl. p. 80.
Wang Cheng-Yi (1959). *Clin. med. J.*, **78**, 257.

AORTIC INCOMPETENCE IN ANKYLOSING SPONDYLITIS

BY

R. S. CROW, M.D., M.R.C.P.
Senior Medical Registrar, Bristol Royal Infirmary

Only recently has it been recognized that patients suffering from ankylosing spondylitis may develop aortic incompetence due to a type of aortitis and aortic endocarditis that has distinctive pathological features. The earliest description of this lesion was given by Mallory *et al.* (1936), but its unique nature and its relationship to joint disease were first recognized by Bauer *et al.* (1951). These workers (Clark *et al.*, 1957) later reported on 22 cases collected over a period of 20 years. Further examples have been recorded by Baker *et al.* (1955), MacMahon *et al.* (1955), Schilder *et al.* (1956), and Toone *et al.* (1959). Ansell *et al.* (1958), giving the first description of the condition in this country, described two cases, with necropsy details of one.

The purpose of this communication is to record the clinical and pathological features of a further case.

Case Report

In 1935 the patient, then a man of 27 with no history of significant previous illness, was passed fit for service in the regular Army. In 1942, at the age of 34, he complained of pain in the back while on a battle course, but continued on full active service as an officer. Three years later he developed painful swelling of the right knee-joint accompanied by pyrexia, followed by pain in other joints and in the back. Radiographs of the spine revealed moderately advanced ankylosing spondylitis.

During the next eight years he continued to serve in the Army, while the joint disease pursued an intermittent progressive course. He received various forms of treatment, including radiotherapy to the spine. In 1949 he had an attack of iritis. In the same year, for the first time in many medical examinations, an apical systolic murmur was noted. This was considered by an experienced physician to be of no pathological significance, and the heart appeared normal on a radiograph of the chest.

In 1954 an exacerbation of spondylitis, with pain in the back, knees, and left shoulder, and with considerable loss of weight, led to his admission to the Queen Alexandra Military Hospital. He was found to have an aortic diastolic murmur, with left ventricular enlargement, collapsing pulse, and high pulse-pressure. There was no evidence of syphilis, and Dr. Evan Bedford thought that the aortic lesion was an example of the aortitis of ankylosing spondylitis.

In 1955 another exacerbation of joint pain and swelling led to his readmission. He now had diminished exercise tolerance and intermittent oedema of the ankles. There was free aortic regurgitation with blowing to-and-fro murmurs in the aortic area, and in addition a low-pitched mitral diastolic murmur. This was thought to be an Austin Flint murmur, as the left auricle was not enlarged.

Thereafter his effort dyspnoea increased rapidly, and in April, 1956, he developed congestive heart failure. The

cardiac murmurs were unchanged, but there were now peripheral circulatory signs of severe aortic incompetence, gross cardiac enlargement, triple rhythm, and intermittent flutter-fibrillation. The heart failure was controlled by treatment and he was invalided from the Army.

He then came under the care of Dr. C. J. Fuller, of the Royal Devon and Exeter Hospital. He complained of stiffness of the back, hips, and shoulders and pain in the right knee. The vertebral column was quite immobile, though with little deformity; there was slight limitation of movement of both hip-joints but full movement of the shoulders; the right knee was swollen, with severe limitation of movement. There was no abnormality of the joints of the hands or feet.

The radiographic features were characteristic of advanced ankylosing spondylitis (Middlemiss, 1956). The summarized findings, as reported by Dr. J. H. Middlemiss, were as follows. The vertebral column throughout its length presented the picture of a typical "bamboo spine" with complete bony ankylosis of the diarthrodial joints and complete bony ossification of the lateral ligaments and the anterior longitudinal ligament. Many of the costo-vertebral joints were ankylosed. In the pelvis, both sacro-iliac joints were completely fused, the symphysis pubis was fused and ossified, and there were typical advanced changes in the ischial tuberosities and the outer aspects of the iliac bones. The hip-joints, the right knee-joint, and the right acromio-clavicular joint showed the non-specific changes of a chronic inflammatory arthritis.

The heart was greatly enlarged, with a forceful left ventricular impulse at the apex. The pulse was regular and collapsing, the blood-pressure 130/30. There were loud aortic systolic and diastolic murmurs, with a palpable aortic systolic thrill. At the apex there was a systolic murmur well conducted into the axilla, and a rumbling diastolic murmur.

He suffered from disabling pain in the affected joints, but there was no change in his cardiac condition until March, 1957, when he suddenly deteriorated with severe dyspnoea and haemoptyses. He was admitted to hospital in severe congestive heart failure, with signs suggesting infarction of the right lower lobe. The cardiac signs were unchanged and the rhythm remained regular. There was no evidence of peripheral venous thrombosis. In spite of vigorous treatment the heart failure increased and he died four days later.

Necropsy Findings

The relevant findings at necropsy were as follows. "There was a slight excess of clear fluid in the pericardial sac. The heart was greatly enlarged (820 g.). On the surface of the heart, near the base of the ventricles, were several blotchy sub-epicardial haemorrhages. Right auricle: moderately enlarged. A small amount of adherent clot was present in the auricular appendage. Tricuspid valve: cusp not thickened; valve dilated and admitting more than four fingers. Pulmonary orifice: moderately dilated. Right ventricle: considerably dilated and muscle slightly thickened. Mitral valve: admitted four fingers and was dilated; both cusps showed chronic thickening, but there was no evidence of stenosis or any indication of either present or old infective endocarditis. Aortic valve: the aortic cusps were thickened and slightly fused. The aortic ring was somewhat enlarged. Most of the thickening noted was behind the cusps on the aortic wall. From the base of the aortic valve for a distance of 2.5 cm. the surface of the aorta was corrugated and showed a raised, smooth, pearly-grey surface. Similar pearly areas were present on the anterior cusp of the mitral valve and on the adjacent aortic cusp. The orifices of both coronary arteries were distorted, but the arteries themselves were free from disease. There was very little aortic atheroma. The condition suggested chronic mitral and aortic endocarditis with incompetence of both valves. The left ventricle was grossly enlarged and the muscle moderately thickened.

"Microscopical examination of the aorta and thickened aortic cusps showed that in the affected area there were thickening and hyalinization of the intima and some fibroblastic proliferation in its deeper part. Many large collections of lymphocytes were present in the adventitia, sufficient in places to give an appearance of lymphadenoid deposits. These collections were sometimes perivascular and sometimes not."

In the lower lobe of the right lung there was a firm haemorrhagic infarct measuring about 4 × 3 cm., and one or two smaller more recent infarcts. The abdominal organs revealed the changes of long-standing chronic venous congestion. The joints were not examined at necropsy.

Comment

This patient had never had acute rheumatism, and there was no history or clinical or pathological evidence of syphilis. He first had symptoms of ankylosing spondylitis at the age of 34, and the diagnosis was made three years later. His heart was thought to be normal until, at the age of 46, in the twelfth year of the disease, aortic incompetence was discovered during an exacerbation of the spondylitis. Effort symptoms developed within two years, and a few months later congestive heart failure supervened. Death occurred from congestive heart failure at the age of 49, little more than three years after the aortic lesion was discovered. The ankylosing spondylitis, which was of at least 16 years' duration, remained active until his death. During its course he had suffered from severe involvement of large peripheral joints which frequently overshadowed the spinal symptoms, and he had one attack of iritis.

Clinical Features

Nearly 40 cases have now been reported of this type of heart disease, of which the present case is a typical example. The clinical features, based on these published accounts, may be summarized as follows.

All the patients have been male. The age of onset of the joint disease, though often not definitely known, has varied from 9 to 51 years, being commonly in the third and fourth decades. The time of onset of the cardiac lesion is also often not precisely known, but it varies from the third to the thirtieth year of the disease, usually being between the tenth and fifteenth years.

Aortic incompetence is thought to appear during exacerbations of the arthritis, sometimes accompanied by pericarditis, and may progress rapidly during subsequent exacerbations. Gleckler (1954) has given an account of a case of acute carditis occurring during an exacerbation of long-standing spondylitis, and it may well be that all cases begin with an acute aortitis and endocarditis which usually escapes recognition. Clinically detectable involvement of the mitral valve rarely occurs, though, as in any severe aortic incompetence, Austin Flint murmurs are a fairly frequent finding.

The aortic lesion has in some cases led to the patient's death within one or two years, but in other instances patients have remained relatively well for 15 years or more (Baker *et al.*, 1955). In general it is progressive, and causes increasing disability within a few years. Angina pectoris, due to deformity of the coronary ostia, is a not uncommon feature, and once it occurs the expectation of life is short. The onset of congestive heart failure also bears a bad prognosis.

In the great majority of cases the ankylosing spondylitis has been accompanied by arthritis of peripheral joints. Many have suffered from attacks of

iritis as an additional complication of their joint disease. Electrocardiographic changes are very common at all stages of the cardiac affection, notably conduction defects varying from prolongation of the P–R interval to complete left bundle-branch block. Auricular fibrillation is a frequent occurrence. The radiological features are those of aortic incompetence in general, but it is most unusual for the aorta to be significantly dilated.

The incidence of this cardiac lesion in cases of spondylitis cannot be assessed with any accuracy, for the clinical diagnosis can never be certain, but it is certainly low. It is probably in the region of 2%. Schilder *et al.* (1956) found five cases in a survey of 100 males suffering from aortic incompetence of varied aetiology.

Pathological Features

Detailed descriptions of the pathological findings in 16 cases have been reported. The most striking macroscopic feature is a curious thickening of the aortic intima and endocardium, usually smooth, glossy, and pearly grey, but in early more active lesions pinker and more granular. It occurs characteristically at the root of the aorta, spreading fanwise upwards from the commissures of the aortic valve (rarely extending more than a few centimetres into the ascending aorta) and downwards over the aortic cusps. Sometimes it extends into the left ventricular endocardium, occasionally reaching the anterior leaflet of the mitral valve. Thickening, rigidity, and distortion of the aortic valve cusps occur, with rolling of their edges but rarely any adherence between them in the commissures. Sometimes there is some dilatation of the aortic ring but usually little separation of the cusps such as occurs in syphilitic aortitis, the regurgitation being due rather to distortion and rigidity of the cusps. In a few cases, where the characteristic endocardial changes have extended into the anterior leaflet of the mitral valve, this has been somewhat thickened, but the mitral valve is not otherwise affected.

The histological features of the aorta resemble those of syphilis. Thickening and hyalinization of the intima occur, with foci of inflammatory cells. In the media focal necrosis, disintegration of the elastica, and fibrosis are present. The adventitia shows fibro-muscular thickening and endarteritis obliterans of the vasa vasorum, with perivascular inflammatory infiltration. In the myocardium, foci of necrosis, interstitial fibrosis, and sometimes endarteritis are found.

Discussion

It is clear from the pathological evidence that the lesion described here is a distinctive type of aortitis and endocarditis which occurs in cases of ankylosing spondylitis. A unique relationship to this disease is, however, not definitely established.

In this country anklyosing spondylitis is regarded as a disease *sui generis*, whereas in the United States it is generally thought to be a variant of rheumatoid arthritis. In American publications it is sometimes accorded separate recognition as "rheumatoid spondylitis," but often no distinction whatever is made. In all the reported cases of this cardiac lesion in which adequate information is given the joint disease has been what, in this country, would be called ankylosing spondylitis. There are, however, a few possible exceptions.

Clark *et al.* (1957) record that "by the usual criteria all but two [of their 22 cases] might be said to have rheumatoid spondylitis," but they give no details of these. Pirani and Bennett (1951) describe a very similar lesion in a case of juvenile rheumatoid arthritis; Levin *et al.* (1955) report "inflammatory lesions of the ascending aorta" in four cases of rheumatoid arthritis (without spondylitis), but these may be a different entity, similar to that described by Cruickshank (1958).

Cruickshank (1958) discusses the cardiac complications of rheumatoid arthritis and their relation to this spondylitic type of lesion. He considers them to be different conditions and calls for the recording of all such cases; "for if the occurrence of distinct lesions in rheumatoid arthritis and ankylosing spondylitis can be conclusively established, this will constitute still further evidence for regarding these conditions as separate entities rather than as varieties of the one disease."

Apart from these few possible exceptions the lesion described here has occurred exclusively in ankylosing spondylitis. The existing evidence suggests that it should be regarded as a visceral complication of this disease.

A high incidence of electrocardiographic and clinical cardiac abnormalities was found in ankylosing spondylitis by Bernstein and Broch (1949) and by Blumberg and Ragan (1956). The former authors, on inadequate grounds, ascribed these to coincident rheumatic heart disease. It seems more likely that there exists a distinct "spondylitic" type of disease of the heart and aorta which in its gross form as described here is rare, but which may occur in lesser degrees more frequently than has been recognized.

Summary

An account is given of the clinical and pathological features of a case in which ankylosing spondylitis was complicated by a distinctive type of aortitis and endocarditis of the aortic and mitral valves. The literature concerning this cardiac lesion is reviewed and its characteristic clinical and pathological features are summarized. The relationship of this lesion to ankylosing spondylitis, and to rheumatoid arthritis and rheumatoid heart disease, is briefly discussed. The existing evidence indicates that it is a visceral manifestation of ankylosing spondylitis.

I am indebted to Dr. C. J. Fuller for permission to publish this case; to Dr. G. Stewart Smith for the description of the pathological findings; to Dr. J. H. Middlemiss for a detailed radiological report; and to Lieutenant Colonel J. P. Baird, R.A.M.C., for a detailed account of the patient's Army medical history.

References

Ansell, B. M., Bywaters, E. G. L., and Doniach, I. (1958). *Brit. Heart J.*, **20**, 507.

Baker, W. H., *et al.* (1955). *Amer. Practit.*, **6**, 1236.

Bauer, W., Clark, W. S., and Kulka, J. P. (1951). *Ann. rheum. Dis.*, **10**, 470.

Bernstein, L., and Broch, O. J. (1949). *Acta med. scand.*, **135**, 185.

Blumberg, B., and Ragan, C. (1956). *Medicine (Baltimore)*, **35**, 1.

Clark, W. S., Kulka, J. P., and Bauer, W. (1957). *Amer. J. Med.*, **22**, 580.

Cruickshank, B. (1958). *J. Path. Bact.*, **76**, 223.

Gleckler, W. J. (1954). *Amer. J. Med.*, **16**, 284.

Levin, M. H., Kaplan, L., Marcus, S., Weinberger, H. J., and Patterson, J. (1955). *Ann. rheum. Dis.*, **14**, 430.

MacMahon, H. E., Magendantz, H., Brugsch, H. G., and Patterson, J. F. (1955). *Bull. Tufts-New Engl. med. Cent.*, **1**, 50.

Mallory, T. B., *et al.* (1936). *New Engl. J. Med.*, **214**, 690.

Middlemiss, J. H. (1956). *J. Fac. Radiol. (Lond.)*, **7**, 155.

Pirani, C. L., and Bennett, G. A. (1951). *Bull. Hosp. Jt Dis. (N.Y.)*, **12**, 335.

Schilder, D. P., Harvey, W. P., and Hufnagel, C. A. (1956). *New Engl. J. Med.*, **255**, 11.

Toone, E. C., Pierce, E. L., and Hennigar, G. R. (1959). *Amer. J. Med.*, **26**, 255.

SPONTANEOUS SUBLUXATION OF THE STERNOCLAVICULAR JOINT

BY

J. G. BONNIN, F.R.C.S., M.R.C.O.G.

Orthopaedic Surgeon, Central Middlesex Hospital, London

Simplicity and innocence appear to be as disarming to the medical author as they are to the novelist, and this explains why no reference to the condition of slow, painless subluxation of the sternoclavicular joint in elderly people has been found in the literature until the appearance of the paper by Bremner (1959). The condition is comparatively common, and an inspection of the neck-line will show inequality in the prominence of the sternal end of the clavicle in many elderly women who are unaware of it and in whom no symptoms arise. In a small group, however, subluxation of the joint becomes so pronounced that the subcutaneous bulge produced by the sternal end of the clavicle is noticed by the patient or arouses suspicions of neoplastic change in the mind of the doctor, and this is the commonest diagnosis encountered when patients are referred to an out-patient clinic.

A Series of Cases

My interest having been aroused, I have kept a record of cases seen, and in two years have been able to collect 11 (see Table). They fall into two distinct groups:

List of Cases

Case No.	Age	Duration of Swelling	Side	Associated Disease	Occupation
1	21	1 month	R	None	Clerk
2	16	1 year	R	,,	Typist
3 (male)	14	Not known	R	,,	Schoolboy
4	15	3 weeks	R	Fracture of right clavicle, aged 2½	,,
5	35	5 months	R	None	Typist
6	81	3 ,,	R	,,	Housewife
7	72	Years	R	Degenerative tendinitis short rotator cuff right shoulder	,,
8	59	5 years	L	Osteoarthritis lumbar spine and hands	,,
9	67		R	Tuberculosis lumbar spine	,,
10	79	Years	R	Spondylolisthesis L 4 on L 5	,,
11	69	5 months	R	Herpes right side of neck and shoulder	,,

(1) the spontaneous subluxation in the elderly (six cases), presumably due to tissue relaxation with age in a joint which is primarily dependent on the strength of the sternocostal ligament for retention; and (2) a group of less obvious cases with mild subluxation seen in adolescents (four cases). With regard to this second group it is difficult to state whether the condition is a mild congenital laxity of the joint and abnormal enlargement of the sternal end of the clavicle, or the end-result of a minor injury—for example, a fracture of the clavicle in childhood—or subacute infection.

In the elderly these cases are nearly all symptomless, but occasionally patients present with a history of some aching pain in the region of the joint, sometimes associated with their occupation—for example, typists. Owing to technical difficulties radiological examination confirms the subluxation only in marked displacement; occasionally it shows evidence of osteoarthritic change and general osteoporosis in the elderly patient, but it adds nothing to explain the cause.

Diagnosis

The differential diagnosis includes tumours of the skin and subcutaneous tissues in the region, which are readily enough excluded. Less easily excluded are congenital anomalies, usually of the first rib, tumours of the inner end of the clavicle (our only recorded case being a Brodie's abscess of tuberculous origin), and subacute infective arthritis. Tumours below the clavicle may produce subluxation. Occasionally there is traumatic dislocation of the sternoclavicular joint, which in spite of treatment is seldom cured and leaves the sternoclavicular joint subluxated but symptomless in most cases (Fig. 1). In the cases noted in the elderly, the right sternoclavicular joint was involved in all but one patient, and she was left-handed. As the condition never presented with acute symptoms, and cases which had been kept under observation showed no change over the years, operative procedures were not carried out. The death of one patient (Case 10) enabled us to examine both sternoclavicular joints, and these showed osteoarthritic changes, with erosion of cartilage and exposed bone. On the right side there was marked degeneration of the intra-articular fibro-cartilage, and communication was established with the sternocostal joint of the right rib on that side (Fig. 2). The sternocostal joint showed osteoarthritic changes similar to those of the sternoclavicular joint. It was filled with an opaque mucous fluid, dirty grey in colour.

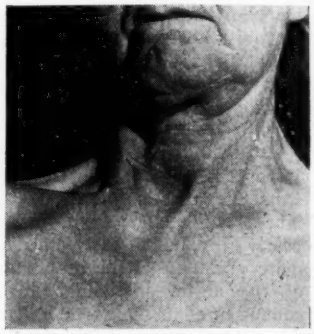


FIG. 1.—Characteristic appearances of a mild subluxation of the right sternoclavicular joint in Case 11.

Histology

Histological examination showed a papillary fibrosynovial proliferation upon which much fibrin and numerous small intra-articular fibrinous bodies were

FIG. 2.—Macroscopic appearances of the right sternoclavicular joint in Case 10. Post-mortem specimen. A, Eroded and degenerate end of the right clavicle. B, Fibro-cartilaginous disk. C, Communication with the sternocostal joint of the first rib, which is also osteoarthritic.

being formed. There were a few lymphocytes, but no evidence of a true infective origin was seen. The articular surfaces were covered by some fibrous overgrowth, but in other places the joint surfaces were eroded and showed degeneration of the cartilage. These changes represent a combination of fibrosis and degenerative change of an osteoarthritic type, and there is a close similarity to the changes reported by Bremner in his series of joints which were explored (R. Drury, personal communication). The pathological changes noted seem to support the view that the condition is primarily one of joint degeneration of an osteoarthritic type, and further support is given by the clinical findings and the harmless and uneventful progress of the cases.

Conclusion

It is apparent that the following conditions may easily be confused, and recognition of the syndrome and its observation enables one to distinguish. (1) Subluxations in adolescence—for example, after childhood fractures of the clavicle, or a congenital defect in or near the joint. (2) Subluxations due to subacute infective arthritis: (*a*) associated with general disease—for example, rheumatoid arthritis; (*b*) monarticular. (3) Subluxation due to degenerative changes in the elderly, affecting the right shoulder in most cases, but possibly the left in left-handed patients, usually symptomless and stationary, but increasing slowly in some cases. These cases appear to be limited entirely to the female sex.

REFERENCE

Bremner, R. A. (1959). *J. Bone Jt Surg.*, 41B, 749.

TWO CASES OF CONGENITAL COMPLETE HEART-BLOCK DIAGNOSED ANTENATALLY

BY

J. EYTON-JONES, M.B., F.R.C.S.Ed., M.R.C.O.G.

Senior Registrar in Obstetrics and Gynaecology, Halifax Group of Hospitals

Congenital abnormalities of the foetus occur in from 1 to 2% of total births, and those affecting the heart are much less common than deformities of the central nervous system. A cardiac defect associated with complete heart-block is rarer still, and, so far as antenatal diagnosis of this condition is concerned, McNie and Johnstone (1959) have remarked on 13 such cases recorded by various authors, and illustrated one of their own due to an interauricular septal defect. Their article, plus the fact that congenital foetal abnormalities are becoming of increasing importance as a cause of stillbirths and neonatal deaths, has prompted me to record two further cases of congenital complete heart-block diagnosed antenatally.

Case 1

A primigravida aged 23 booked for hospital confinement when 12 weeks pregnant. Her family and previous medical history showed nothing of importance and all routine investigations were normal. A threatened miscarriage at 18 weeks necessitated a week's stay in hospital. Apart from this the pregnancy was uneventful until she was admitted in very early labour at 38 weeks by her dates. I was called to see her on account of a slow foetal heart rate.

On abdominal examination the uterus was small for the dates, but the presentation was vertex, back to the left, and the head was deeply engaged in the pelvis. The uterus was soft and no tenderness was elicited. Slight contractions, one in 15 minutes, were noted. The foetal heart rate was only 40 a minute but quite regular, and this rate was maintained during continuous auscultation for several minutes. On vaginal examination the cervix was effaced, dilated one fingerbreadth, and well applied to the head, which was in mid-cavity. The membranes were intact, no cord was felt, and bleeding was absent. Her blood-pressure was 130/70 mm. Hg, urine examination was negative, and there was no evidence of oedema. Perusal of the antenatal card showed that she had last been seen two weeks previously, when everything had been satisfactory; but all previous observers had relied on the presence of foetal movements to confirm a living foetus.

In the absence of any obvious cause of foetal distress and because of the very slow regular heart rate, I made a tentative diagnosis of congenital cardiac abnormality with complete heart-block, and allowed labour to proceed. The first stage lasted four and a half hours and the second stage half an hour, ending in a vaginal vertex delivery after a small episiotomy. The membranes ruptured at full dilatation of the cervix and the liquor was clear. Throughout the labour the foetal heart rate remained regular at 36 to 42 a minute. Finally the third stage was normal, lasting 10 minutes, and inspection of the placenta and membranes showed no abnormality.

The infant, a female weighing 5 lb. 12 oz. (2,608 g.), cried well at birth, dispelling initial cyanosis. Results of investigations were as follows: haemoglobin, 129%; white cell count, 9,200/c.mm. Film showed nothing of note. *X*-ray examination of chest showed generalized enlargement of the heart shadow, indicating a congenital cardiac malformation; no evidence of lung disease. Electrocardiogram showed complete auriculo-ventricular dissociation, with regular QRS complexes at 42 a minute. Clinically the infant showed no cyanosis and no murmur was heard. It was thought that the likeliest cause of the block was a septal defect and that the prognosis was poor. The infant was artificially fed and was discharged with the mother 10 days after delivery, having regained her birth weight. During this time her condition gave rise to no anxiety and the heart rate was stable at 40 a minute.

Subsequent Progress.—When 3 weeks old the infant was readmitted to the children's ward as the mother stated the baby was crying and did not feed properly. The weight was now 6 lb. 2 oz. (2,778 g.), but there was still no cyanosis or cardiac murmur, and the heart rate remained at 42 a minute. Despite routine care the infant's condition gradually deteriorated, with increasing poor colour at feeding times, and death occurred at the age of 6 weeks. Unfortunately permission for a post-mortem was not obtained.

Case 2

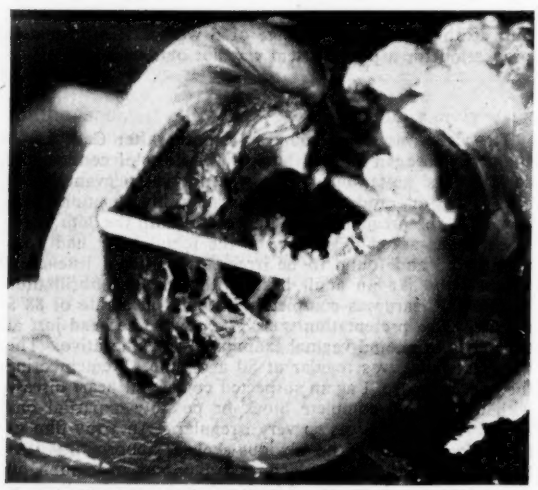
This case was noted some six months after Case 1. A primigravida aged 19 was booked for hospital confinement at 19 weeks' gestation. There was nothing relevant in the medical history, and all routine antenatal investigations were normal. The pregnancy was uneventful until the 36th week, when I was asked to see her as the foetal heart had been auscultated and found to be irregular. When I listened it was exactly like an adult heart with auricular fibrillation. The foetal heart was completely irregular at a rate of 88 a minute. The presentation was vertex, with the head just at the pelvic brim, and vaginal examination was negative. The maternal pulse was regular at 80 a minute. Remembering the previous case, I again suspected congenital heart disease with a probable complete block or possibly a partial one as the foetal heart was so very irregular. An *x*-ray film of the abdomen showed no obvious skeletal abnormality. As the hospital had recently acquired a phonocardiograph an attempt was made to record both a foetal electrocardiogram and phonocardiogram, using the epigastric-suprapubic positions for the suction electrodes as suggested by Southern (1954). Though tracings were obtained it was

extremely doubtful whether an accurate interpretation of them could be made, and they have therefore not been reproduced.

The patient was seen by me weekly thereafter, and at each visit the extreme irregularity of the foetal heart was noted, with on one occasion perfectly coupled beats at a rate of 88 a minute. Labour started spontaneously two days after her calculated date. The first stage lasted 10 hours 40 minutes, the membranes rupturing early, with the drainage of clear liquor, and a vaginal examination excluded any prolapse of the cord. During the first stage the foetal heart varied in rate from 54 to 96 a minute and was always irregular, the slower rates being recorded during a contraction. Vaginal examination 20 minutes after full dilatation of the cervix showed a right occipito-posterior position of the vertex on the ischial spines, so labour was terminated by rotation and forceps under local pudendal block. It was an easy delivery and the third stage was normal, the total labour having lasted 11 hours 10 minutes.

The infant, a mature female weighing 7 lb. 10 oz. (3,465 g.), was deeply cyanosed at birth, and regular respiration was established after routine extraction of mucus and administration of oxygen. Despite the onset of respiration, she remained cyanosed and became more so on crying. When placed in continuous oxygen, however, the cyanosis became much less marked, and after improvement in her general condition various investigations were carried out. Haemoglobin, 95%; red cell count, 4,650,000/c.mm.; white cell count, 32,500/c.mm. Film showed anisocytosis, polychromasia, and some basophilic stippling. Nucleated red cells 67/100 leucocytes. *X*-ray examination of the chest revealed gross generalized enlargement of the heart shadow, suggesting a severe congenital defect; lungs normal. Electrocardiogram showed complete auriculo-ventricular dissociation with multifocal ventricular systoles. The idioventricular rate was 48 a minute. In addition clinical examination detected the presence of an upper abdominal tumour, dull to percussion, which extended mainly into the left hypochondrium, three fingerbreadths below the left costal margin. In view of the probable cardiac lesion it was thought the tumour was a grossly enlarged liver. No murmur was heard on auscultating the heart, which was irregular at 72 a minute. The infant's condition was never really satisfactory despite continuous oxygen, and she died 38 hours after birth.

Post-mortem Report.—The body, that of a normally developed neonate, showed no external evidence of congenital abnormalities. *Abdomen:* Situs inversus of all the abdominal organs was present; the liver was large and showed chronic venous congestion. The right lobe was responsible for the tumour felt in the left hypochondrium. *Cardiovascular System:* The heart was enlarged with hypertrophy and dilatation of both ventricles; a large defect was seen in the membranous part of the interventricular septum and also in the interauricular septum, with partial fusion of mitral and tricuspid valves (see Fig.). The appearances are those of persistent atrioventricularis communis. No abnormality was noted in any other systems. *Cause of Death:* Persistent atrioventricularis communis with situs inversus of abdominal organs.



Case 2. Persistent atrioventricularis communis. The heart has been opened through the anterior wall of the left ventricle and atrium, and the large defect can be seen with the fringe of mitral valve crossing the defect to fuse with the tricuspid. Beyond the defect are the right atrium and ventricle.

Comment

From the anatomical position of the auriculo-ventricular node and main bundle of His, one would expect defects affecting that part of the heart to be associated with congenital complete heart-block. Indeed, Taussig (1947) states that auricular and high ventricular septal defects and also persistent atrioventricularis communis have all been found in such an association. This latter defect was the one discovered in Case 2, and it is also interesting to note that Taussig describes situs inversus with laevocardia; but in her cases the cardiac abnormality was much more complicated. Case 1 would, of course, never have been recorded on its own, as there was no necropsy, but, with Case 2 appearing so soon afterwards, Case 1 has been included for its clinical interest.

So far as the antenatal diagnosis of congenital complete heart-block is concerned, the finding, on more than one occasion, of a persistently slow foetal heart which approaches the idioventricular rate could hardly be anything else. The much commoner causes of foetal bradycardia such as prolapsed cord, premature separation of the placenta, strong uterine action, and difficult labours should be excluded with ease by routine investigation, and I have never by chance auscultated a foetal heart at the moment of intrauterine death in those cases where that event has taken place before term. However, the diagnosis of completeness can only be tentative unless a successful foetal electrocardiogram is obtained, because partial blocks of 2 to 1 or 3 to 1 ratios would cause confusion if only auscultation were relied on.

Finally, the presence of congenital complete heart-block, with its almost certainly associated cardiac malformation and usually poor prognosis if the heart rate is under 50 a minute, cannot have any influence *per se* on the management of pregnancy and labour, excepting perhaps a policy of shortening the second stage with forceps if conditions for this operation are favourable.

Summary

Two cases of congenital complete heart-block, in which a tentative diagnosis was made antenatally and confirmed after birth by electrocardiography, are described. The cardiac defect, in the case where a post-mortem examination was made, was persistent atrioventricularis communis, and this was associated with situs inversus of the abdominal viscera.

I am grateful to Mr. Norman Emblin for permission to publish these cases, to Dr. A. T. Edwards for the post-mortem report and the dissection of the specimen in Case 2, and to Dr. D. M. Broughton for the photograph.

REFERENCES

McNie, T. McG., and Johnstone, G. M. (1959). *J. Obstet. Gynaec. Brit. Emp.*, **66**, 135.
Southern, E. M. (1954). Ibid., **61**, 233.
Taussig, H. B. (1947). *Congenital Malformations of the Heart*, pp. 384, 513, 523. Commonwealth Fund, New York.

Medical Memoranda

A First-aid Treatment of Minor Burns

Treatment of minor burns has always presented a problem in general practice. This is shown by the number of treatments which have come and gone; for instance, carron oil in the dim and distant past, picric acid, tannic acid, petrolatum gauze, sodium bicarbonate, and now cortisone ointment.

A simple domestic remedy is presented which is always available at home, does no harm if the burn turns out to be worse than expected, provides prompt relief of pain, and appears to exert a considerable influence on the course of events within its range of utility.

It was discovered accidentally by the patient in Case 1 in 1947. So far as I can ascertain, it is not generally known and has not been recorded, and I have used it in general practice ever since.

Method.—The affected part should be immersed in milk immediately after the burn has occurred. It must be immersed before serious blister formation has occurred. Immersion should continue until the pain has subsided and there has been a regression of any rudimentary blister. This is easy where the hands are involved, but it is difficult to immerse a foot, for instance, in sufficient milk. This can be overcome by using the milk as a cold compress, but the results are less reliable and it entails more trouble (see Case 4). When the affected part gets greasy from the fat in the milk it should be gently wiped with cotton-wool and reimmersed.

ILLUSTRATIVE CASES

Case 1.—A housewife aged 38 was bottling fruit, when some spilt on the dorsum of her left hand. Finding nothing else available, she plunged it into a jug of milk while she telephoned for advice. One and a half hours later she arrived at the surgery, and the only sign of the burn was some erythema and oedema.

Case 2.—A housewife aged 28 was making jam, when some was upset on her left hand. She telephoned for advice and then immersed it in milk (an unfortunate delay). After four hours the hand showed only erythema and oedema, but no pain.

Case 3.—A girl aged 15 scalded her hand and wrist with boiling water while making tea. She was given instructions by telephone. After two hours her hand showed only erythema and slight oedema, but the part of her wrist not covered by milk showed a typical second-degree burn which took two weeks to heal.

Case 4.—A boy aged 6 was looking through the ash-pit of the kitchen cooker, when a gust of wind caused the flames to blow back. He was burnt on the forehead and nose, with singeing of the hair and eyebrows. He was treated immediately with repeated cold compresses of milk. At the end of one and a half hours all that remained was some erythema of the affected part.

Case 5.—I inadvertently picked up the wrong end of an electric soldering-iron. My hand was obviously quite badly burnt on the palm and fingers, and there was the characteristic smell of scorched skin. After two and a half hours of immersion in milk, during which time blister formation was obvious, there remained only some erythema, slight oedema, and flattening of the epidermal ridges. A full day's work was done the next day without any discomfort or difficulty.

Case 6.—A small child aged 3 put his hand on a hotplate of an electric stove, and the mother was instructed in the usual way. After two hours of immersion there was scarcely any visible sign of damage except the erythema.

COMMENT

The treatment outlined here is purely of a first-aid nature, and no pretentious claims are made for it. It is suitable only for scalds and burns of first and second degree; it is not suitable for deep burns and those from electricity or chemicals. Success depends upon immersion within a few minutes of the accident, before any serious blister formation has occurred. This should be continued until pain and blisters have subsided, in order to achieve the aim, which, from a domestic point of view, should be the ability to use the part in a few hours without any dressing.

Cooling a burn to relieve the pain is a logical treatment to the lay mind and dates from antiquity. It has been used medically and investigated in recent times (Courtice, 1946; Langohr *et al.*, 1949).

It was claimed by Langohr *et al.* that it greatly reduced the oedema, possibly by diversion of the blood away from damaged capillaries, and thereby avoiding the effects of capillary stasis.

Milk is a colloidal solution containing about 12.6% of proteins, fat, and salts. It follows, therefore, that a burn will not raise the temperature of milk as quickly as that of an equivalent amount of water. Furthermore, according to Sevitt (1957), the protein concentration of the oedema and blisters varies with the severity of the burn, and it may even approach the serum concentration of 8–9% of solid matter. Thus, there could be an osmotic effect which may be assisted by the damaged epidermis.

I have been unable to find any previous reference to the use of a colloid to reduce tissue oedema in burns in order to prevent blister formation. Immersion in a cold colloid seems to produce a phase of regression in the normal sequence of events.

The prompt relief of pain makes this an invaluable treatment with children, and the absence of any "procedures" avoids considerable psychological trauma.

In view of the results obtained from local immersion in cold colloids, further technical investigations seem merited to find out if it could be applied in a more manageable form for larger or less accessible burns.

CONCLUSION

The conventional treatments for minor burns are designed as aids to healing after the damage has occurred; the treatment here described appears to exert a limiting action on the injury process.

As a first-aid measure, milk is readily available where the majority of minor burns occur—in the kitchen; it can be applied by the patient immediately; it is clean; and, as it can be used afterwards, the cost is negligible.

This treatment has been highly successful in a rural general practice for 11 years, so its wider use seems indicated.

F. L. WILLINGTON, M.B.,
Yelverton, S. Devon.

REFERENCES

Courtice, F. C. (1946). *J. Physiol. (Lond.)*, **104**, 321.
Langohr, J. L., Rosenfeld, L., Owen, C. R., and Cope, O. (1949). *Arch. Surg. (Chicago)*, **59**, 17.
Sevitt, S. (1957). *Burns: Pathology and Therapeutic Applications.* Butterworth, London.

Reviews

SURGICAL TEXTBOOK

Textbook of British Surgery. Edited by Sir Henry Souttar, C.B.E., D.M.(Oxon.), F.R.C.S., and J. C. Goligher, Ch.M. (Edin.), F.R.C.S. (Edin. and Eng.). Volume IV. (Pp. 699 +viii; illustrated. £5 5s.) London: William Heinemann, Medical Books, Ltd. 1959.

The fourth and final volume of the *Textbook of British Surgery,* edited by Sir Henry Souttar and Professor Goligher, has now been published, and it is pleasing to record that the high general standard achieved in the previous volumes has been well maintained. This especially applies to the excellent balance between, and uniformity of presentation of, the various sections, for which the editors—aided this time by Mr. Norman Capener—deserve great praise.

The new volume is in essence an orthopaedic textbook, but chapters are included on infections, burns, and accidental wounds. The whole is of the highest merit, while the names of the various eminent writers are a guarantee that the teaching is authoritative.

The book runs to 700 pages and there are no fewer than 405 illustrations, some of them line drawings of great clarity and value. As one would expect from the nature of the subject, there are a large number of radiographs, and here the universally recognized difficulty of reproducing by the half-tone process the subtle and delicate bony changes shown in the original films reveals itself. This is particularly noticeable in the chapter on bone tumours; it is, of course, much less significant when mechanical derangements are illustrated. This is not meant to be a criticism of this book in particular, for the defect is due to the process itself and can only be overcome, and then not completely, by very costly methods and by the use of highest grade art paper; when a large number of plates have to be produced, this would be economically impossible.

The final chapter on amputations includes a very useful section on artificial limbs which fills a hiatus sometimes found in the knowledge of the examination candidate. It is indeed, according to the preface, especially for these candidates that this work was produced, and we have no hesitation in saying that it fulfils that purpose very adequately. It is impossible to imagine that a candidate who has absorbed all that is here to be found could conceivably fail in his higher examinations.

NORMAN C. LAKE.

OBSTETRIC ANAESTHESIA

Principles and Practice of Obstetric Anaesthesia. By J. Selwyn Crawford, M.B., Ch.B., D.A.(Eng.), F.F.A.R.C.S. (Pp. 128. 20s.) Oxford: Blackwell Scientific Publications. 1959.

There will be much support for the author's plea that obstetric anaesthesia should be taken more seriously. It is a branch of anaesthesia needing, and deserving, special study and attention. It will also be felt to be appropriate that a good deal of space has been given to descriptions of the physiological processes concerned, both maternal and foetal, and if there is disagreement over some small points this is not surprising, since theories are changing all the time. Resuscitation of the newborn, a subject of great interest to the obstetric anaesthetist, receives due consideration. In this, as in other matters, the author may perhaps have been influenced by his residence in the United States. As the two chief inhalation anaesthetic agents for forceps delivery and caesarean section he offers ether and cyclopropane, and states that "dominant opinion in Britain is probably still in favour of ether as the mainstay in obstetric practice." This may be so, but it would be interesting to know what would be the result of an inquiry. One gets the impression that in private homes chloroform is still quite widely used, whereas in many hospitals a frequent prescription is nitrous oxide and oxygen using a high proportion of oxygen, supplemented by a muscle relaxant—succinyl-choline or tubarine—and perhaps a little ether or cyclopropane as well, and preceded by one of various methods of induction. Standardization, however, would be very dull, and there is plenty of good material in this book to stimulate thought and discussion. Indeed, this is probably the most informative and up-to-date work on obstetric anaesthesia at the present time.

In common with most books on obstetric anaesthesia it contains a section on "obstetric analgesia." This has come to be expected of an author, and by tradition it consists of a recital of the use of some drugs, with perhaps a sentence or two on the need for "reassurance." This does not give a true picture of our present understanding of the relief of pain in labour. Drugs play their part and anaesthetists have made valuable contributions of their effective utilization—one has only to recall Dr. Minnitt to provide an outstanding example. They continue to do so, but, as Dr. Crawford reminds us, the anaesthetist serves best when he is integrated as part of a team. Analgesic drugs are most useful when used with full regard for the other important measures necessary to the mother's comfort and contentment. Perhaps future accounts will show even more clearly the true perspective on these matters.

SHÎLA RANSOM.

CHOLERA

Cholera. By R. Pollitzer, M.D. With two chapters written in collaboration with W. Burrows, M.D., and S. Swaroop, Ph.D., M.P.H. (Pp. 1,019; illustrated. £5.) Geneva: World Health Organization. London: H.M. Stationery Office. 1959.

The author of this massive monograph writes with an authority derived from a long first-hand acquaintance with the subject. The main part of the work, which was written at the invitation of the World Health Organization, appeared originally in eleven separate articles published in the *Bulletin* of that organization. These have now been revised and brought up to date. To summarize such a book in the brief space of a review is an impossible task. The various chapters give comprehensive accounts, each supported by an exhaustive list of references, of the history of the disease, world incidence, bacteriology, immunology, bacteriophage investigations, general pathology, laboratory diagnosis, clinical pathology, symptomatology, diagnosis, prognosis and treatment, epidemiology, prevention and control, with an appendix on suspect stool examination. This is, in fact, an up-to-date and complete work of reference, in which each section is a compilation of the findings of different workers. These findings are not infrequently at variance, and, although the author interpolates cautious opinions, readers may feel that the value of the book would be increased if at the end of each

chapter the author summarized the points which had been discussed, and drew, where applicable, the conclusions which he considered justifiable.

It is interesting to note that replacement of body fluids by means of saline infusions remains the sheet-anchor of treatment. Essential oils, kaolin, and potassium permanganate, all of which had their enthusiastic advocates, have failed to stand the test of time. Serotherapy is ineffective, bacteriophage has been abandoned, and newer remedies, such as sulphonamides and antibiotics, confer little if any significant benefit. In prophylaxis, while bacteriophage has not fulfilled the claims once made for it, evidence is accumulating to show that vaccination is of value. But the secret of prevention still lies in the implementation of sanitary measures, and in particular the provision of safe water supplies.

J. S. K. BOYD.

COALMINER'S PNEUMOCONIOSIS

La Tuberculose des Houilleurs. By Jacques Prignot. (Pp. 327; illustrated.) Brussels: Editions Arscia S.A. 1959.

Our knowledge of coalminer's pneumoconiosis, though greatly advanced, is still far from complete. The clinical problems arising from the association of tuberculosis and pneumoconiosis in coalminers are of considerable significance in Belgium.

The author of this book reports on 180 cases of what he calls infective pulmonary tuberculosis in coalminers who had worked underground for more than five years, and his study comprises a large number of control cases of non-infective pneumoconiosis. He divides his infective cases into four groups: (1) simple pneumoconiosis with non-cavitating tuberculosis; (2) simple pneumoconiosis with cavitating tuberculosis; (3) progressive massive fibrosis (P.M.F.) with non-cavitating tuberculosis; and (4) P.M.F. with cavitating tuberculosis. His study involves comprehensive clinical, radiological, haematological, bacteriological, macroscopic, and microscopic examinations, and, in addition, bronchoscopy was performed in 105 cases of pneumoconiosis, 55 of which were of infective tuberculosis. Radiological examination, including tomography, formed an important part of diagnosis, and the results of medical treatment with two or three of the routine antibiotic drugs were studied in 89 of the infective cases. It was noted that the radiological shadows showed little tendency to resolution, massive shadows sometimes progressing during treatment. Of these cases, 57 became quiescent, though 24 required surgical resection. In 22 the disease remained active and in 10 there was a fatal issue.

It is generally agreed in this country that the changes seen radiologically in coalminers can be classified into simple pneumoconiosis and P.M.F. The former, a benign condition, shows generalized minute opacities, depending on the degree of dust exposure, whereas in the rather larger opacities, which tend to increase and fuse, they form larger massive shadows even if dust exposure is no longer present.

In Prignot's study, 103 of his 180 cases of P.M.F. were found to have tubercle bacilli, but the tuberculosis was more frequently of the cavitating type. Cochrane and his colleagues in 1954 found that only 1% of cases of P.M.F. had a positive sputum, and in these the prognosis was grave, but the recognized similarity between tuberculosis and P.M.F., radiologically and pathologically, together with the finding of up to 40% of positive T.B. cultures by Gough and his colleagues in a consecutive series of necropsies on miners with P.M.F., is certainly significant.

In summary, it would appear to be generally accepted that in simple pneumoconiosis where miners are exposed to relatively low dust concentration the mortality is low. Where the concentration is higher the prevalence of tuberculosis and pneumoconiosis is correspondingly increased.

This book is well produced, the illustrations throughout are good, and one is pleased to note the large number of beautiful coloured sections of lungs from Professor Gough's department in Cardiff, as well as the recognition shown of the exceptional work done by his department and by the pneumoconiosis research unit of the Medical Research Council at Llandough Hospital. The bibliography is extensive and its thoroughly international flavour is greatly welcome.

PHILIP ELLMAN.

⁂ This review was written shortly before Dr. Ellman's death.

GENIUS IN MIDDLE LIFE

The Gifted Group at Mid-Life. Thirty-five Years' Follow-up of the Superior Child. By Lewis M. Terman and Melita H. Oden. (Pp. 155+xiii; illustrated. 36s.) Stanford, California: Stanford University Press. London: Oxford University Press.

This book is the fifth of the *Genetic Studies of Genius*, nearly all of which have been concerned with the follow-up of 1,000 gifted children, originally tested in California in 1921. The present volume reports the latest follow-up study carried out 35 years after the original testing of the children. Professor Terman was in the mid-forties when the study began and most of the children were about 11. When he died near the end of his eightieth year the "children" had reached their mid-forties. Future investigations of this group will be carried out by Robert R. Sears, who points out in his foreword that "on actuarial grounds there is considerable likelihood that the last of Terman's Gifted Children would not have yielded the last report to the files before the year 2010!" The present book is rather shorter than the previous ones, and it can be read by itself, as it contains an adequate if brief description of previous work done on this group. The main outcome can be described in relatively few words. The group of superior children has become an adult group "superior in nearly every aspect to the generality. . . . The superiority of the group is greatest in intellectual ability, in scholastic accomplishment, and in vocational achievements. Physically the gifted subjects continue to be above average as shown in their lower mortality record and in the health ratings. . . . The group does not differ greatly from the generality in the extent of personality and adjustment problems . . . the incidence of such other problems as excessive use of liquor (alcoholism) and homosexuality is below that found in the total population, and the delinquency rate is quite a small fraction of that in the generality." The documentation for these conclusions is thorough and detailed and will be of considerable interest to most readers. Terman believes that the group has by no means yet reached its highest level of achievement, in terms of either status or income, and it is difficult to disagree with him on this. It is particularly interesting to note that the

members of the group have actually increased in intelligence, as measured in terms of the concept mastery test, "increases occurring in all educational and occupational levels, in all grades of ability and at all ages. The data indicate that not only do the mentally superior hold their own, but that they actually increase in intellectual stature."

Two other points of interest may be singled out. Sex differences are pronounced so far as achievement is concerned. Although the women in the sample have considerable achievements to their credit, nevertheless, the majority do not compare with the male half of the sample, but find their achievement essentially in the home. The other point of interest is related to the causes of failure in this mentally superior sample. These seem to lie in temperamental factors related to the notion of neuroticism, those lacking in achievement being characterized by lack of persistence, lack of integration, lack of self-confidence, and the possession of inferiority feelings. The existence of these temperamental differences between failures and successes was notable even at an early age.

If there is one criticism to be made of this truly remarkable study, it must lie in the fact that the Gifted Group is constantly contrasted with what Terman calls the "Generality." This is not an appropriate comparison in most cases, as the gifted children were not only intellectually superior, but also came from middle- and upper-class homes in the majority of cases. Thus the effects of intelligence and social class are confounded in the analysis. Additional analyses related to the social origins of the superior group might have been of considerable value in elucidating this point.

H. J. EYSENCK.

MIDDLE EAR

The Middle Ear. By Heinrich G. Kobrak. Foreword by John R. Lindsay. (Pp. 254+xvi; illustrated. £5 12s. 6d.) Chicago: University of Chicago Press. London: Cambridge University Press. 1959.

Now that it has become fashionable to write more and more about less and less, a book which deals only with the middle ear should not come as a surprise.

Edited by the late Dr. H. Kobrak, whose untimely death in November, 1957, robbed the world of a very ingenious and versatile research worker, the first part of this work consists largely of his experimental work on the transmission of sound across the middle ear. Some of this has not been described before, and it is indeed a fitting memorial to his research. Included in this part are some interesting accounts of early work in this field.

The second part of the book is devoted to the treatment of conductive deafness by surgical measures, and consists of a series of articles by acknowledged experts in this field. Dr. John Lindsay writes on otosclerosis and fenestration, Dr. S. Rosen on mobilization of the stapes and fenestration of the oval window, while Professor H. Wullstein and Professor F. Zollner each contribute a chapter on their work on the plastic repair of the sound-conducting system of the middle ear. Much of what is in this book can be read elsewhere, but Dr. Kobrak's account of his own investigations should be read by all who contemplate experimental investigation of middle ear function.

TERENCE CAWTHORNE.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Biochemische Befunde in der Differential-diagnose Innerer Krankheiten. By H. U. Anton, P. Doering, W. Eger, E. Fritze, S. Hollmann, H. Karte, H. Kellner, R. Schoen, G. Schulze, M. Schwab, and H. Südhof. Edited by R. Schoen and H. Südhof. (Pp. 493+xvi; illustrated. DM. 58.) Stuttgart: Georg Thieme Verlag. 1960.

Lehrbuch der Gynäkologie. By Professor Dr. Heinrich Martius. Sixth edition. (Pp. 432+xvi; illustrated. DM. 54.) Stuttgart: Georg Thieme Verlag. 1960.

Einführung in die Psychiatrie. By Kurt Kolle. (Pp. 92. DM. 6.80) Stuttgart: Georg Thieme Verlag. 1960.

Advances in Psychosomatic Medicine. Edited by A. Jores and B. Stokvis. Volume I: ***Symposium of the Fourth European Conference on Psychosomatic Research, Hamburg, April 1959.*** Edited by A. Jores and H. Freyberger. (Pp. 330+x; illustrated. Sw.fr. 58.) Basle, New York: S. Karger. 1960.

Studies on the Technique of Skin Testing in Allergy. By W. J. F. van der Bijl, M.D. (Pp. 100+viii; illustrated. Fl.12.50.) Leyden: H. E. Stenfert Kroese N.V. 1960.

Fermente-Hormone-Vitamine: und die Beziehungen Dieser Wirkstoffe Zueinander. Volume II. ***Hormone.*** Edited by Robert Ammon and Wilhelm Dirscherl, with 14 contributors. Third edition. (Pp. 897+xxiv; illustrated. DM. 148.) Stuttgart: Georg Thieme Verlag. 1960.

Studies in Radiotherapeutics. By J. S. Mitchell, C.B.E., M.D., F.R.S. (Pp. 274+vii; illustrated. 52s. 6d.) Oxford: Blackwell Scientific Publications. 1960.

The Population Explosion and Christian Responsibility. By Richard M. Fagley. (Pp. 260+ix. 28s.) New York and London: Oxford University Press. 1960.

Living Animal Material for Biological Research. Proceedings of a Symposium organized by the International Committee on Laboratory Animals, October 6-9, 1958. Edited by W. Lane-Petter. (Pp. 100. 20s.) Obtainable from: Secretary-General, I.C.L.A., Woodmansterne Road, Carshalton, Surrey. 1960.

An Introduction to Human Blood Groups. By Fulton Roberts, M.D. (Pp. 85+viii. 9s. 6d.) London: William Heinemann (Medical Books) Ltd. 1960.

The Origins of Love and Hate. By Ian D. Suttie. (Pp. 222. 3s 6d.) Harmondsworth: Penguin Books. 1960.

Homosexuality. By D. J. West. (Pp. 200. 3s. 6d.) Harmondsworth: Penguin Books. 1960.

Lecture Notes on Ophthalmology. By Patrick D. Trevor-Roper, M.A., M.D., B.Chir.(Cantab.), F.R.C.S., D.O.M.S.(Eng.). (Pp. 94+v; illustrated. 12s. 6d.) Oxford: Blackwell Scientific Publications, 1960.

The Photography of Patients: Including Discussions of Basic Photographic and Optical Principles and Infrared Techniques. By H. Lou Gibson, F.B.P.A., F.P.S.A. Second edition. (Pp. 200+ix; illustrated. 84s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Bibliographical Citation. By Cyril C. Barnard. Second edition. (Pp. 20. 2s. 6d.) London: James Clarke and Co., Ltd.

Spirit Healing. By Harry Edwards. (Pp. 173; illustrated. 18s.) London: Herbert Jenkins. 1960.

Xylocaine. The Pharmacological Basis of its Clinical Use. By Sten Wiedling. (Pp. 146; illustrated. Sw.kr. 20.) Stockholm: Almqvist and Wiksell. 1959.

Thymectomy for Myasthenia Gravis. A Record of Experiences at the Massachusetts General Hospital. By Henry R. Viets, M.D., and Robert S. Schwab, M.D. (Pp. 143+xv; illustrated. 56s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Surgical Gastroenterology. Considerations based on Pathologic Physiology. By Warner F. Bowers, A.B., B.Sc., M.D., M.Sc., Ph.D.(Surg.). Medical Illustrations by George J. Thomas, A.B., M.Med.Art. (Pp. 498+xii. £7 8s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Transactions of the Ophthalmological Society of the United Kingdom. Volume LXXIX. Session 1959. (Pp. 780+lxxi; illustrated.) London: J. and A. Churchill, Ltd. 1960.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY JULY 23 1960

ADOLESCENCE

When, about the beginning of this century, the public conscience began to be concerned over the welfare of young people, it found expression first in measures to reduce the heavy mortality of infancy and in efforts to improve the well-being of toddlers and school-children. More recently, especially since the end of the second world war, increasing thought has been given to the problems of adolescence. This interest has been stimulated in part by the impact on society of what is sometimes a rather turbulent period of adaptation and in part by a growing recognition that much can be done to help the adolescent. One difficulty cramping work in this field lay in lack of information about the normal course of adolescence and, in particular, about how young people fared after they left school—how easily they settled into suitable work, how soon they found their feet in society, how many ran into trouble with the police, and so on. By large-scale study much material was in time collected,[1] but in these days of rapid change some of it has already become obsolete, and there is need for a running audit designed to furnish information about changes in contemporary environment and the reactions of young people to them. Recent work has shown that there were considerable changes in the leisure activities of secondary-school children between 1947 and 1958. In Ilford,[2] for example, many more children began to join clubs: now among 15-year-old modern-school pupils about 80% of boys and 53% of girls belong to youth clubs, mixed clubs being favoured. Scout and Guide membership, on the other hand, has fallen by fully 50% among modern-school pupils and even more among those at grammar schools. The proportion of young people attending cinemas has fallen, but, on the other hand, some 67% of all 15-year-old school-children now have record-players or radiograms at home and 88% include listening to records among their leisure pursuits. It seems that modern children are distinguished at play from their predecessors by an urge to read adult periodicals, to dance, to listen to records, and to talk with children of their own age in clubs, cafés and other places where they feel relatively free from the restrictive influence of adults. This urge to be independent, to be grown-up at an earlier age than their predecessors, may be due possibly to the earlier onset of puberty and is encouraged by the higher standard of living which has given to young people a purchasing power unimagined by their predecessors ten years ago and not passing unnoticed by commercial interests.

The problems of adolescents are not, in the main, problems of physical disability, though there is some evidence that dental decay is much more prevalent than it ought to be, and that, especially among girls, faulty posture and abnormalities of the feet which some attribute to the wearing of unsuitable shoes give cause for concern. The physical strain associated with going to work is not, as a rule, too great, though the heavy industries have problems of their own and in some areas travelling adds to the demands of the working day. Young people themselves rarely appreciate the need for rest.

The medical and social problems of adolescence was the subject chosen for review by the discussion groups which have been formed, with the Council's encouragement, by many B.M.A. Divisions. Some of the groups produced admirable reports of their deliberations, and all these emphasized the importance of wholesome family life in the development of the child, particularly in his early years. There was a general feeling that the chief source of antisocial behaviour in adolescence lay in lowered standards of parental control. It may be national environment rather than youth that has changed: as one Division (Winchester) put it:

> "The society in which to-day's adolescents find themselves is one of bewildering change . . . the speed of life is greater, competition and specialization have increased *pari passu* with a decrease in moral safeguards, and the advent of the welfare state has provided a national cushion against responsibility and adversity. . . . The growth of a sense of responsibility competent to influence adolescent behaviour will take more than one generation."

Certainly many of the troubles of youth spring from ignorance and misunderstanding and failure in the family circle. Home life must be interesting and worth while, as well as providing food and shelter: the home circle should be patently interested in the adolescent's activities and problems.

Though youth organizations provide no effective substitute for good home background they have a valuable part to play in directing the excess energy of adolescents into healthy channels and, in the

[1] Ferguson, T., and Cunnison, J., *The Young Wage Earner*, 1951. Published for the Nuffield Foundation by the Oxford University Press.
[2] Stewart, Mary, *The Leisure Activities of School Children*, 1960. The Workers Educational Association, London.
[3] Leading article in *J. Amer. med. Ass.*, 1960, **172**, 1291.

process, effectively reducing antisocial behaviour. In new housing areas, particularly, with their tendency to disruption of old ties, facilities of this type should be provided before the adolescent is tempted to drift to less desirable activities. The emphasis should be on self-help as well as on active participation in recreational pursuits. The success of a youth club is very largely a measure of the success of its leader, and suitable people should be encouraged to take up youth leadership as a worth-while career. Some believe that youth clubs should have scholastic, religious, or political affiliations rather than a civic background and organization, believing that then they are likely to have a greater sense of purpose and continuity. The drift away from such clubs about the age of 16 can only be regretted when, as sometimes happens, the club is replaced as a focal point for social activity by the public house. Will the raising of the minimum school-leaving age to 16 ease the problems of adolescence? There is some reason to believe that raising the age to 15 created almost as many social problems as it solved, and careful thought must be given to the curriculum of the additional year if further extension is not to be productive of further frustration.

Fortunately most adolescents overcome their problems. There is no reason to believe that young people to-day are of poorer material than their predecessors or that they are not making reasonable use of their opportunities. Few require psychiatric care or even the ministrations of "teenage clinics" of the type established in Boston in 1952, where once again it has been observed that the changes accompanying even normal development can frighten some children and puzzle their parents.[3] But some, and not merely the demonstrably handicapped, require more help than is available at present. Doctors, along with parents, with the Church, with education authorities, and indeed with all active social agencies, have a responsibility in helping to create a background compatible with the healthy development of young people.

CAUSES OF PERNICIOUS ANAEMIA

Defective haemopoiesis with macrocytic anaemia and megaloblastic bone-marrow may arise from many causes. The common variety of this disorder, Addisonian pernicious anaemia, has long been recognized to be a consequence of degeneration of the gastric mucosa, with loss of secretion of intrinsic factor and failure to absorb vitamin B_{12}. Why does the initial mucosal degeneration develop? Do nutritional, environmental, or infective factors play a causative part, or is hereditary predisposition paramount? To these old questions newer methods of investigation have not yet yielded unequivocal answers. Indeed, we may reflect a little ruefully that our modern techniques of augmented histamine testing, tubeless gastric analysis, assays of vitamin B_{12} in serum, measurements of absorption and excretion of radioactive vitamin B_{12}, and biopsy of the gastric mucosa, though they have taught us much about non-Addisonian megaloblastic anaemias, and have proved valuable in diagnosis and in confirming certain older hypotheses on pathogenesis, have contributed surprisingly little to our knowledge of the fundamental causes of pernicious anaemia. Nevertheless, data from which answers may yet be found continue to accumulate.

Remarkable variations in the incidence of pernicious anaemia among different races and in different geographical locations have been known for many years to exist, though they have not been precisely measured. The disease is commonest among peoples from the temperate zones and especially in races like the Scandinavians, with a tendency to fair hair and blue eyes. It is much less common in Italians, Russians, and Jews, is rare in negroes, and still rarer in Orientals. Comprehensive information on the prevalence of pernicious anaemia in different localities within the same country has not hitherto been available, though in Sweden the incidence appears to be greatest in the central regions,[1] and in North America higher in Canada, the Great Lakes, and New England than in the Southern States.[2] Regional variations in Great Britain have now been assessed in a pilot survey conducted by the College of General Practitioners with the help of family doctors from 4,700 practices throughout the country, dealing with a population of over 16 million. The results of this collective investigation have recently been reported by E. Scott.[3] For Great Britain as a whole the rate was 1.27 per thousand, but it varied between 2.46 per thousand in Banff and Elgin to 0.60 per thousand in Hertfordshire. The general pattern of incidence showed decreasing prevalence from north-west to south-east, with rates for large cities similar

[1] Nordensen, N. G., Segerdahl, E., Strandell, B., and Wallman-Carlsson, C., *Acta med. scand.*, 1938, **97**, 222.
[2] Wintrobe, M. M., *Clinical Hematology*, 1956, 4th ed., p. 467, London.
[3] Scott, E., *J. Coll. Gen. Pract.*, 1960, **3**, 80.
[4] Meulengracht, E., *Amer. J. med. Sci.*, 1925, **169**, 177.
[5] Neel, J. V., *Medicine (Baltimore)*, 1947, **26**, 115.
[6] Mosbech, J., *Heredity in Perniclous Anaemia*, 1953, Copenhagen.
[7] Callender, S. T., and Denborough, M. A., *Brit. J. Haemat.*, 1957, **3**, 88.
[8] McIntyre, P. A., Hahn, R., Conley, C. L., and Glass, B., *Bull. Johns Hopk. Hosp.*, 1959, **104**, 309.
[9] Witts, L. J., *Proceedings of the 7th Congress of the European Society of Haematology, London*, 1959, in press, Basel.
[10] —— *Med. Serv. J.*, 1959, **15**, 645.
[11] Murphy, W. P., *Anaemia in Practice*, 1939, Philadelphia and London, p. 210.
[12] Verel, D., Turnbull, A., Tudhope, G. R., and Ross, J. H., *Quart. J. Med.*, 1959, **28**, 491.

to those for their neighbouring counties. The regularity of this gradient is striking, but the explanation for it is not obvious. Possibilities mentioned by Scott include a correlation with past unemployment and presumable malnutrition in the industrial north, and a relationship to geological ground structure. But the geology of the country is so complex, with many mountains of sedimentary rock lying near those of volcanic origin, that no clear relationship between geological formation and incidence of this disease is apparent. Inequalities in distribution of persons of blood group A, who are known to have a slightly higher incidence of the disease, do not explain the variations, since group A is least common in the north and west. Perhaps the most likely explanation lies in familial predisposition.

Earlier views on the importance of a hereditary factor in pernicious anaemia[4–6] have received strong support from recent investigations of the secretion of intrinsic factor by relatives of patients with the disease. S. T. Callender and M. A. Denborough[7] showed that such relatives commonly have a deficiency of intrinsic factor, and P. A. McIntyre and her colleagues[8] found defective secretion in no less than 21% of 100 relatives of patients with pernicious anaemia whose capacity to absorb vitamin B_{12} was measured by the Schilling test. On the basis of observations of this kind, L. J. Witts[9 10] has suggested that latent pernicious anaemia is much commoner than the overt disease.

We may therefore draw a tentative picture of pernicious anaemia as a familial disease caused primarily by the possession of a gene of low penetrance, which is responsible for a slowly progressive degeneration of the gastric mucosa. This degeneration occurs usually but not invariably in the later years of life, and is associated with a loss of intrinsic factor sufficient to cause anaemia in only a small proportion of those suffering from it.

Even if future studies confirm this hypothesis, the possibility still remains that other factors may hasten the development of the gastric lesions in susceptible patients. Pernicious anaemia is more common in women than in men, as are gastritis and states of iron deficiency, and these latter abnormalities may accelerate mucosal degeneration. Defective nutrition might act similarly, and so might states of psychological stress, as W. P. Murphy emphasized many years ago.[11] Endogenous factors may also play a part, since disorders of thyroid secretion appear to be associated with an increased incidence of pernicious anaemia.[12] There is still, clearly, much to be learned about this common disease.

THE REAL ACTORS

On the scale of cosmic evolution, the three centuries that have passed since the Royal Society was founded "are as nothing." While opening his Tercentenary Address last Tuesday on this note, Sir Cyril Hinshelwood, O.M., P.R.S., went on to express what must be the animating thought of many scientists—"In achievement the 300 years have exceeded all the infinite wastes of evolutionary time: by the scale of human events they are the fullest and longest in all existence."

In last week's issue of the *Journal*, as well as in many other publications celebrating the tercentenary of the Royal Society's foundation, historians have shown how fortunate Great Britain was in that remarkable collection of men who came together at a crucial time. Sir Cyril has this to say: "These men, in whom the elements were thus diversely mixed, initiated the humane tradition of the Society, the union of thought and action, the partnership between men of the study and men of the world, which has been maintained throughout its existence, is preserved, we would like to hope, to-day, and will decide its future." The distinctive feature of the men, and latterly women also, who have composed the Royal Society has been their originality, a quality somewhat sparsely distributed in the population. "Let us have no illusions about one thing," says Hinshelwood, "to-day we commemorate the doings of a minority, and of a small minority." And again, "only minorities in general exercise an independent taste and judgment or produce original thought." Against this background the difficulty that the members of such an academy must sometimes feel in granting their Fellowship is evident: "And as Nature herself takes infinite pains over the perpetuation of the species, making this indeed in most respect her first concern, so the right choice of its members is a matter demanding the most anxious care of the academy, and is perhaps the most important thing it has to do."

In discussing the part science has played in changing the face of the world, Sir Cyril raises the question whether we have yet got this into the right perspective. "From the time of the foundation of the Royal Society onwards there was a steady increase in the number of dedicated men who by the concentration of their minds, the skill of their hands, and the sweat of their brow worked to uncover the secrets of nature. Their labours were largely unknown to their contemporaries, they are but perfunctorily recorded by historians, and yet they have ended by transforming the face of the globe and

the life of humanity." But he goes on: "Most conventional history records the waxing and waning of political movements, the course of wars, and the fate of dynastic ambitions. These have been deemed the proper material for polite studies. The adventure and achievements of science have seldom been vouchsafed the attention of the chronicler, nor has their study usually been rated as humane. Yet they have not only transformed the conditions of life but they are the product of human genius, and above all of the determination, sacrifice, and devotion of men, who must on that account be deemed among the foremost representatives of their day." Many educationists are at present concerned about the gulf between scientific and humane studies in the schools and universities, so that perhaps not too many decades will pass before historians and other interpreters of the human scene find a grounding in scientific method a help to their understanding of it.

It is not to be wondered at that the President of the Royal Society, himself a highly original scientist, should lay stress on the individual: "The real actors in the drama of these centuries have been individuals, often rare individuals." He asks the question: "What then in it all has really been the role of the Royal Society as a corporate body?" In answering this he touches on problems that are at the centre of our civilization to-day:

"Scientific investigation needs material ways and means, and the further knowledge advances the more lavish becomes the scale. The individual in isolation becomes, except under rare conditions, correspondingly impotent. But the community as a social and political whole cannot be expected to possess the detailed understanding to support him. Nor, to-day, with the tremendous issues at stake can it remain indifferent. What therefore must be created to mediate between the individual and the major group is a specialized minor community large enough to command prestige and confidence, but with membership confined to those who place the claims of knowledge first. The principles which should govern the constitution of such a body are highly important.

"Specialized organs of the Government are by themselves unsafe, being too exposed to the changing winds of expediency. Universities suffer from the disadvantage that on the one hand a given branch of knowledge is divided and scattered among many of them, and on the other hand that they have competing preoccupations of importance to them commensurate with that of learning.

"An academy therefore is the natural body to provide for several vital things, non-commercial periodicals for the publication of discoveries, a measure of financial support for ideas still too embryonic to be of immediately obvious practical application, the mutual stimulus of association and discussion, and the immaterial reward of honour for intellectual achievement. Governments may act as patrons. They can and do solicit and receive the help of learned men, they favour and encourage enterprises which they judge to be timely, but they cannot provide for men of science the intangible yet powerful encouragement which comes from acceptance and election by their peers. The academy, if it maintains high standards of unquestioned impartiality, sets the tone throughout the scientific community, and its influence is felt in every quarter. It is no rival to Government organizations or to industry, and should maintain the closest connexions with them by electing into its number the leaders from both. Because men of action and men of authority esteem it an honour to be elected, the academy exerts its influence far beyond the confines of the learned world. The professional men of science hear of the needs of the state and of industry, which in their turn are irrigated by the currents of scientific thought. The intercourse on terms of equality between the representatives of these different estates of the nation is like a sensitive nervous mechanism endowing the community which possess it with capacities and potentialities realizable in no other way. The subtle co-ordinating action of an academy can no more be replaced by a bureaucratic organization or a system of economic incentives and deterrents than the intricately evolved biological controls of a living organism can be replaced by crudely devised mechanical appliances."

Sir Cyril returns to the unique individual in the framework provided by the community in which he lives and works: "It is the duty of the Royal Society not to predict, not to legislate, but to maintain within the larger community the smaller one in which creative activity can flourish. Its members owe a multiplicity of loyalties, none of which can be fulfilled without the others: to mankind in general, to their native land, and to the Royal Society itself. But that is not all, for there are communities in time as well as space. The most original minds, in some sense isolated in all contemporary groupings, find their true affinities in continuing the sequence of their predecessors, and their fulfilment only in their successors. In a measure this is true not only of genius but of all men. It is what moves us in history. It is what the honouring of this occasion means."

MEASLES AND DISTEMPER

Resemblances between human measles and canine distemper have often been discussed since H. Pinkerton and his colleagues[1] noted similar histopathological changes in giant-cell pneumonia, distemper, and measles. Characteristic multinucleated giant cells containing intranuclear and cytoplasmic inclusion bodies are found in tissues and in tissue cultures infected by either virus.[2–6] J. M. Adams[7] and D. T. Karzon[8] studied neutralization of egg-adapted distemper virus by human sera and gamma globulin: the neutralizing factor had an age distribution like that of antibody to a common human viral infection, and it

was found to develop in cases of measles. These findings have been confirmed and extended by G. Carlström,[9-12] who adapted distemper virus to suckling mice and used these animals to detect and measure neutralizing antibodies. Carlström also noted the presence of distemper-neutralizing antibodies in the sera of young children in Iceland, where canine distemper had not been recognized for the previous 12 years. By adapting measles virus to suckling mice Carlström[13] made it possible for the first time to perform cross-neutralization tests between measles and distemper viruses in the same experimental system. The viruses were shown to be immunologically related, but, while distemper antiserum neutralized both viruses equally, antiserum to measles was about 25 times more potent against measles than against distemper virus. This difference was found consistently with antisera prepared in different species and with human measles-convalescent sera.

On pathological, immunological, and epidemiological grounds the viruses of measles and canine distemper appear to be closely related but not identical. Carlström[11] proposes a new virus group containing the three viruses of measles, distemper, and rinderpest (which is serologically related to distemper[14 15]). Although distemper-neutralizing antibodies in human sera are usually due to antecedent measles infection, it is interesting to speculate whether other viruses of the group may occasionally infect man and give rise to such antibodies.

F. L. Black[16] found measles antibodies in the unexpectedly high proportion of 12 out of 37 subjects of an average age of 6.9 years with no history of measles in earlier life. Although this might be attributable to defective memories or missed diagnoses, it remains possible that some of the antibodies were due to infections with a virus other than measles but antigenically related to it. Could this be distemper? Could this be the cause of some cases of minor respiratory illness, non-bacterial pneumonitis, or giant-cell pneumonia, as suspected by Pinkerton[1] and Adams[7]? If so, the occurrence appears to be uncommon, since evidence to support such a hypothesis has not yet emerged from the many intensive virological studies of acute respiratory diseases now in progress in many countries of the world.

[1] Pinkerton, H., Smiley, W. L., and Anderson, W. A. D., *Amer. J. Path.*, 1945, **21**, 1.
[2] Adams, J. M., Imagawa, D. T., Yoshimori, M., and Huntington, R. W., *Pediatrics*, 1956, **18**, 888.
[3] Enders, J. F., and Peebles, T. C., *Proc. Soc. exp. Biol. Med.*, 1954, **86**, 27
[4] Ruckle, G., *J. Immunol.*, 1957, **78**, 330.
[5] Rockborn, G., *Arch. ges. Virusforsch.*, 1958, **8**, 485.
[6] Vantsis, J. T., *Vet. Rec.*, 1959, **71**, 99.
[7] Adams, J. M., *Pediatrics*, 1953, **11**, 15.
[8] Karzon, D. T., ibid., 1955, **16**, 809.
[9] Carlström, G., *Acta Paediat.*, 1956, **45**, 180.
[10] —— *Lancet*, 1957, **2**, 344.
[11] —— *Acta Paediat.*, 1959, **48**, 25.
[12] —— *Arch. ges. Virusforsch.*, 1959, **8**, 539.
[13] —— ibid., 1959, **8**, 527.
[14] Polding, J. B., and Simpson, R. M., *Vet. Rec.*, 1957, **69**, 582.
[15] Goret, P., Mornet, P., Gilbert, Y., and Pilet, C., *C.R. Acad. Sci. (Paris)*, 1957, **245**, 2564.
[16] Black, F. L., *J. Immunol.*, 1959, **83**, 74.

ARTIFICIAL TAN

The capacity of a substance known as D.H.A. (for dihydroxyacetone, or 1,3-dihydroxy 2-propanone) to give a "sun-tanned" appearance to the skin has been exploited in cosmetic preparations. One recently put on the British market is sold as an after-shave lotion—presumably to make it acceptable to the conservative male.[1] The manufacturers advise that the lotion be applied three or four times at hourly intervals during the course of an evening and thereafter once daily to maintain the "tan." P. B. Mumford[2] investigated the response to applications of a 2.5% solution of D.H.A. He found that light brown pigmentation developed six to ten hours after a single application and that with repeated applications a light negroid tint was obtained. The colour is not removed by cleaning agents or fat solvents, but gradually fades over the course of seven to ten days as a result of the normal shedding of the horny layer. Mumford found that the delay between application of the lotion and the appearance of pigmentation made it difficult to obtain a uniform intensity of colour, and a streaky pattern was sometimes produced. No irritation or discomfort was noted in either normal or eczematous subjects.

D.H.A. occurs very widely in nature. Its phosphate is formed as one of the stages in the breakdown of carbohydrates in both animals and plants. The substance may be prepared synthetically by the controlled oxidation of glycerol, but for its commercial production the conversion of glycerol by micro-organisms, usually species of *Aerobacter*, is generally preferred. The availability of D.H.A. at an economic price has revived interest in its possible therapeutic and industrial application. A highly reactive molecule, D.H.A. has been shown to have antiviral activity, and nitrogenous derivatives are said to have antituberculous properties. Condensation of D.H.A. with sulphonamides yields water-soluble resins, for which many industrial uses are foreseen. Combination with amino-acids, followed by polymerization, gives rise to a brown product known as melanoidin or humin, which is responsible both for the discoloration of fruit juices and for the dark stain which may form on the teeth after ingestion of soluble carbohydrates. It is this brown pigment which is formed when D.H.A. is applied to the skin, the hydroxyl radicals of D.H.A. combining with amino-acids in keratin.

The commercial preparation is said to have provoked some allergic dermatitis,[1] but on the available evidence it is not certain that the D.H.A. rather than some other ingredient of the lotion was responsible. A potential and probably greater hazard is that the user will unjustifiably assume that his "tan" will give him as much protection from sunlight as a natural tan, whereas in fact it gives none.

It is too early to predict whether Englishmen will take kindly to a synthetic "tan" and whether, if they do, these potential hazards will prove to be of any real

[1] Bryce, D. M., *Pharm. J.*, 1960, **184**, 491.
[2] Mumford, P. B., *Brit. J. Derm.*, 1960, **72**, 279.

clinical significance. But they are worth bearing in mind. Dermatologists might take up Mumford's suggestion that D.H.A. may, with some modification of the available preparation, be useful in the treatment of vitiligo, in which the methoxypsoralens have proved unreliable.

NEW CLINICAL RESEARCH CENTRE

The Medical Research Council is to establish a large Clinical Research Centre, with up to 200 beds, in an existing hospital, probably in London. It should be working in two or three years' time. Its director will be Professor J. R. Squire, at present Leith professor of experimental pathology at Birmingham, and it will have a full-time research staff of 50–60 doctors and scientists. It is hoped, later, to appoint part-time workers who would prefer to combine the practice of medicine with the conduct of a certain amount of research. The new Centre will be the clinical counterpart of the Council's "preclinical" National Institute for Medical Research, and will be located reasonably near it.

Announcing this news at a press conference on Tuesday, Sir Harold Himsworth said that the Centre was intended to fill a gap in the Council's resources for clinical research—which he defined as "research in contact with patients." At present, he said, the Council used training awards, "project" grants, and small research units attached to hospitals for this type of work. But there was nothing comparable to the National Institute for mounting major research attacks in the clinical field. This deficiency the new Centre would remedy.

Wisely the Council has set its face firmly against any suggestion of a separate research hospital. The new Centre is to form part of an existing 500–700-bedded hospital providing a full range of services to the community. It was important, said Sir Harold, to keep research in contact with current practice, and if the proportion of research beds to total complement exceeded one-third, then the nature of the hospital would change and the important contact between practice and research would be lost. Another function possible in a large centre like this, but not in a small unit, was that new groupings of medical and scientific specialties could be tried out in response to new research needs.

As yet there is no blue-print for the Centre. Experience, the personal interests of its director and staff, and the research problems uncovered will all influence its development. The first phase will be concerned with setting up the basic departments—internal medicine, pathology, microbiology, clinical chemistry, and clinical physics were Sir Harold's list. After that other units will be grafted on as occasion dictates. Professor Squire's own research interests include immunology and renal disease, and it would not be surprising, therefore, if these were to feature in the Centre's future programme. At all events this venture is well in the tradition of practical farsightedness for which the British Medical Research Council has long been famous.

WRONG PRESCRIPTION

Last week some of the national newspapers went to town on a new drug recently introduced from the U.S.A. into Great Britain by Roche Products. It is methaminodiazepoxide, with the proprietary name "librium," and in virtue of a sedative action is intended for use in psychotherapy. Newspaper readers were regaled with pictures of snarling lynxes and told that the drug made them calm—even "calm as a baby," said one reporter in a glow of paternal recollection. Since our neighbours, colleagues, competitors, and family seem all too often to be animated by a lynx-like ferocity, the popular appeal of such a drug is clear to those who write for an audience numbered in millions. But what is clearer to medical men is the danger of such publicity. Experience has shown time and again that the uncritical lauding of a new drug or operation raises hopes that are inexorably dashed sooner or later. In this case, too, the drug is said to be obtainable without prescription from chemists, though they will no doubt act with caution if people ask for it over the counter, especially as the manufacturers have recommended that it be taken only on a doctor's prescription.

According to the advertising literature sent to professional people, librium is said by its manufacturers to be "unique," "chemically in a class by itself," "pharmacologically in a class by itself," "clinically in a class by itself." Evidently a promising drug—like many others. A series of papers on it by American authors[1] suggests that it gives a sense of well-being to patients in addition to acting as a sedative. It is reported to have been beneficial in the treatment of patients with anxiety and tension. No doubt it will be tried out further in the U.S.A. and other countries; in Great Britain trials are already under way. Meanwhile the publicizing of this preparation might be all the better if confined to professional channels, and many doctors must regret that Roche Products felt their hand so forced by publicity in one newspaper that they held a press conference which resulted in further publicity in others.

P.R.C.S.

Sir Arthur Porritt has been elected President of the Royal College of Surgeons in succession to Sir James Paterson Ross, who has held that office since 1957. A New Zealander and a former Olympic athlete, Sir Arthur is serjeant-surgeon to the Queen, and, among his hospital appointments, is surgeon to St. Mary's. This year he succeeded the Prince Philip, Duke of Edinburgh, as President of the British Medical Association. It is, we believe, the first time that any man has been simultaneously the President of the B.M.A. and of the R.C.S.

[1] Symposium on Newer Antidepressant and Other Psychotherapeutic Drugs, *Dis. nerv. Syst.*, 1960, **21**, Suppl.

Clinicopathological Conference

A CASE OF TEMPORAL ARTERITIS

DEMONSTRATED AT THE

POSTGRADUATE MEDICAL SCHOOL OF LONDON

This is a typical example of "giant-cell" arteritis. Between 1943 and 1959 the patient was admitted on seven occasions to Hammersmith Hospital, where finally he died with cerebral complications (Case No. 185,550; P.M. No. 8,694).

Clinical History

Dr. C. L. COPE: The patient we are considering to-day was a widower aged 70 when he died in February, 1959. Our first records of him are in 1943, when he was admitted for the first time complaining of cough, vomiting, and haematuria. Right lower-lobe pneumonia and pyelitis were diagnosed, and during this illness the blood urea rose to 51 mg. Sulphapyridine was given, and an apical systolic murmur was reported as being present. Blood pressure was 150/110. In 1951 he was seen again for cough and bronchitis. Honeycombing of the right lung base was evident on *x*-ray examination. The left ventricle was enlarged, there was a systolic bruit at the apex, and the blood pressure was 180/110. His second admission was in April, 1956, when he gave a history that seven weeks previously he had begun to feel weak, cold, and shivery, and had started to lose weight. This was followed by several days of persistent hiccup, and of pain in the right knee. Three weeks before admission there had been a short period of melaena lasting four days, and also pain behind the right ear, spreading as severe pain to the back of the head, the neck, and shoulders. There followed acute pain in both temporal regions. There were no visual changes.

TEMPORAL ARTERITIS DIAGNOSED

On examination he was found to be ill, pale, and to have some oedema of the ankles. He had an irregular fever around 100° F. (37.8° C.). Both temporal arteries were thickened and very tender. There was no superficial redness, but neither artery was pulsating above the temporo-mandibular joint. The occipital arteries were not palpable, nor were they tender. Arteries in both arms and legs seemed normal. The left fundus showed a small, punctate haemorrhage; the right was normal. Haemoglobin was 75%; blood urea 46 mg. The sedimentation rate was 82 mm. at one hour.

The diagnosis of temporal arteritis was clear. The patient's headaches and temporal tenderness were severe, and treatment with corticotrophin was started promptly. The response was good; there was marked clinical improvement within 24 hours. Arterial tenderness subsided, and the sedimentation rate fell to 6 mm. The stools were free of occult blood. Radiographs of the spine showed marked cervical spondylosis, though symptoms due to this were probably mild. The patient was discharged 24 days after admission. For a time he continued symptom-free as an out-patient. In early June (1956) temporal pulsation had returned 1½ in. (3.7 cm.) above the temporo-mandibular joint, and by the end of the month there was pulsation 2 in. (5 cm.) above. Throughout this time he was maintained on cortisone 25 mg. twice daily. At the end of July he began to get short of breath on exertion. Blood pressure was 170/125. His face was rather fuller, but he had no oedema and no rise of jugular venous pressure. E.C.G. showed evidence of left ventricular hypertrophy only. Cortisone therapy was halved, and in early August stopped completely. But by mid-August he was again unwell. There was a sudden onset of retrosternal pain with difficulty of breathing. Blood pressure was 230/130. There was a triple rhythm, but no rise of jugular venous pressure. He continued at work until August 16. On that day he experienced sudden pain in the umbilical region on rising from his midday meal. He continued at work until sent home by his manager. The same evening, after going to bed, he experienced sudden stabbing pain in both sides of the chest, in the umbilical region, and between his shoulders. The pain was made worse by deep inspiration, and its site was affected by his position in bed. There was sweating, shivering, and nausea, and the pain lasted all night with little relief.

PROGRESSIVE AORTIC DILATATION

When admitted, his blood pressure was 200/105, but the jugular pressure was not raised. Triple rhythm was present. An E.C.G. showed mild changes, reported as compatible with an antero-septal infarct and/or combined ventricular hypertrophy, and later E.C.G.s did not clarify the picture. The attack was considered probably to be due to a cardiac infarct, but the widespread reference of the pain and the persistence of hypertension raised the possibility of an aortic dissecting aneurysm. Anticoagulant therapy was started. A few days later the superior mediastinal shadow appeared widened at *x*-ray (Fig. 1 (*b*)), and anticoagulant therapy was stopped. During September, 1956, dilatation of the aortic arch became progressively more apparent and a diagnosis of either dissecting aneurysm or giant-cell arteritis of the aortic arch was made, with, probably, associated cardiac infarction. During this time the arm pulses remained symmetrical, but during the month there were three recurrences of severe pain with collapse. In two of these mild left ventricular failure occurred, though there was no associated E.C.G. change. In one attack the blood pressure dropped to 115/90, and the sedimentation rate rose to 70 mm. From these stormy episodes the patient eventually recovered sufficiently to be sent to convalescence on October 18. He continued fairly well for some months, though with some shortness of breath. It is of interest that his blood pressure was only 130/80 in November, 1956.

PROSTATIC OBSTRUCTION

His fourth admission was in March, 1957, because of sudden dyspnoea and haemoptysis. Pulmonary infarction was suspected but not proved. There was some acute bronchitis. The blood pressure was still 130/80. The apical harsh systolic murmur was unchanged. Blood urea was 60 mg., and mild prostatic obstruction was found. He was discharged on April 10. Through early summer he was fairly well, though there was another slight haemoptysis. In July there was

marked shortness of breath on micturition attributed to prostatic obstruction, and this necessitated his fifth admission (July, 1957) to a surgical ward. After a slow bladder-decompression, he had a suprapubic cystostomy. At this time there was partial Cheyne–Stokes breathing, a presystolic gallop, and a normal jugular venous pressure. A month later a transurethral resection of prostate was done, and this was repeated five weeks later. During this latter operation his blood pressure fluctuated widely between 245/140 and 60/0, settling post-operatively at 130/80. He was discharged on October 20 and continued in fairly good condition over the winter. There was still some increased frequency of micturition and also dyspnoea on micturition, but the blood urea had fallen to 27 mg.

The sixth admission occurred in March, 1958, because of an attack of left ventricular failure. The blood pressure was 120/70. The heart was enlarged; there was pulsus alternans and a triple rhythm. The liver was enlarged 3 cm., but there was no oedema and the jugular venous pressure was not raised. The systolic murmur was easily audible in apical and aortic areas. The urine contained pus cells in large numbers, and culture grew *Proteus* and *Bact. coli*. The blood urea had risen to 71 mg. This urinary infection was treated with sulphadimidine and chloramphenicol. He recovered, and was discharged home in three weeks. He continued fairly well, though feeling weak and with poor exercise tolerance, until January, 1959, when there was a return of his malaise.

TERMINAL ILLNESS

On February 2, 1959, he was discovered in deep coma in the coalhouse of his home. At this seventh and final admission he was found to have a right hemiplegia. Head and eyes were deviated to the left. His pulse was 120. Brachial blood pressure was 90/60 on the right and 80/55 on the left. The left carotid was easily palpable, but the right carotid was not felt, though when the blood pressure subsequently rose, the right carotid was as readily felt as the left. Femoral pulses were equal, but the dorsales pedis were not felt. The plantar responses were extensor, and there were crepitations at the left lower zone. He remained in coma, though the blood pressure improved to 110/70. E.C.G. showed no evidence of recent myocardial infarction, and both serum transaminases were normal. The patient died without recovering consciousness on February 7.

Clinical Diagnosis

(1) Thrombosis of left middle cerebral artery.

(2) Temporal arteritis with "giant-cell" arteritis of aorta.

(3) Left ventricular failure.

(4) A possible old antero-septal infarct.

(5) Transurethral prostatic resection.

(6) Possible pyelonephritis.

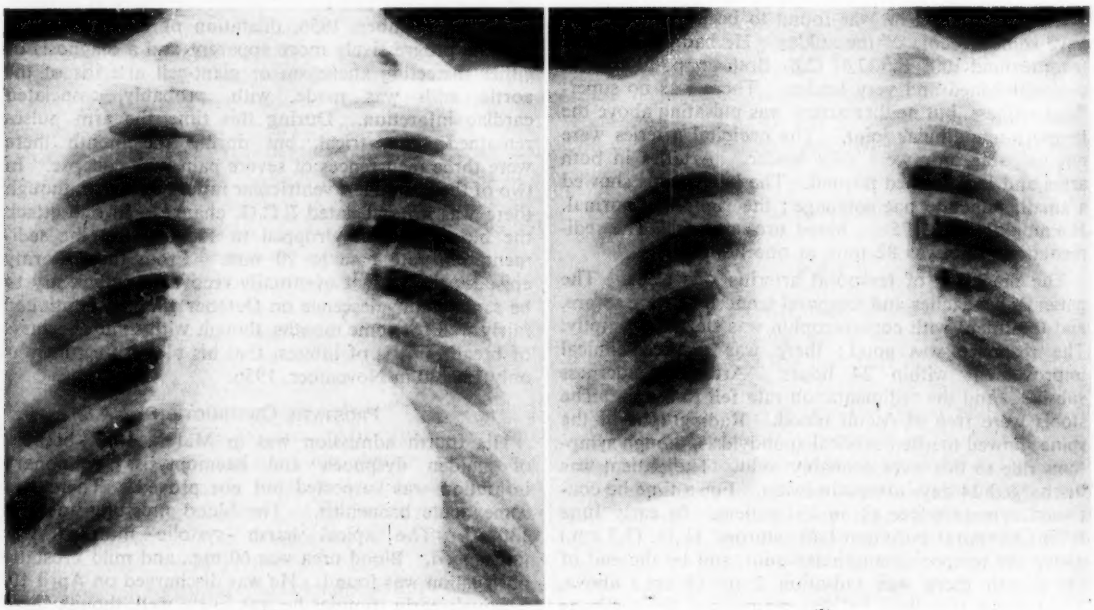
(7) Chronic bronchitis with terminal pneumonia.

(8) Long-standing aortic sclerosis.

Post-mortem Findings

Professor C. V. HARRISON: The body was that of a thin, elderly man (5 ft. 8 in. in height, 111 lb. in weight —1.7 m.; 50 kg.), with a suprapubic scar and a small bed-sore.

The *heart* was enlarged owing to left ventricular hypertrophy. There was a little thickening, apparently atherosclerotic, in the *mitral* and *aortic cusps*. The *coronary arteries* were relatively well-preserved, and there was no macroscopic fibrosis of the muscle. The *aorta* was dilated (93 mm. circumference in arch). Thirty mm. from the base of the aortic valve was a healed dissection (Figs. 2 and 3). There was a horizontal tear 25 mm. long with slight dissection undermining one edge and a localized bulge. In the descending thoracic aorta was a saccular aneurysm on the posterior wall 35 by 20 mm. and 15 mm. deep (Fig. 4). This was filled with old thrombus. Just below the saccular aneurysm



(*a*) (*b*)

FIG. 1.—Postero-anterior radiographs of chest (*a*) on April 23, 1956, and (*b*) on August 18, 1956, showing dilatation of the aortic arch in (*b*).

FIG. 2.—Ascending aorta showing edge of small dissection (marked with arrow) on its left-hand border. (×1.125.)

FIG. 3.—Microscopical details of edge of dissection seen in Fig. 2. At the foot of the picture is the remaining outer part of the aortic wall covered on its inner aspect by a new layer of thickened intima. The lip of the dissection is seen above and is again covered by newly grown intima. Normal aorta is seen right at the top of the picture. (×9.)

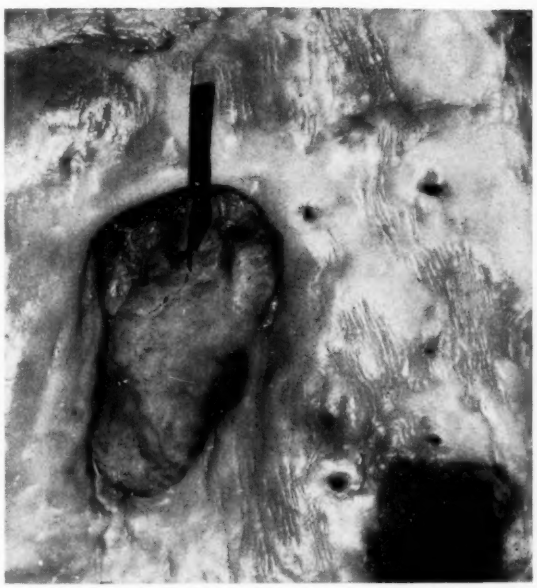


FIG. 4.—Descending thoracic aorta showing saccular aneurysm filled with thrombus (a section has been taken from its upper border). There is mural thrombus over a patch of aortitis (bottom right). (×1.36.)

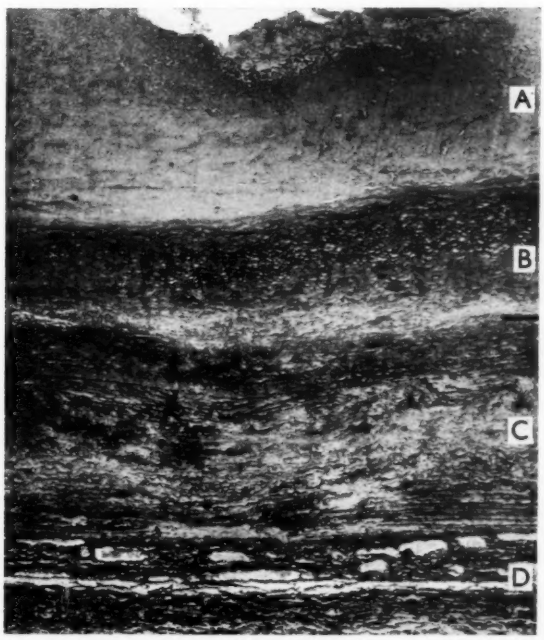


FIG. 5.—Photomicrograph of descending thoracic aorta showing details of the mural thrombus in the lower right-hand corner of Fig. 4. The layers from above downwards are: A, thrombus; B, thickened intima; C, media showing gross destruction of elastic tissue; D, adventitia. (×40.)

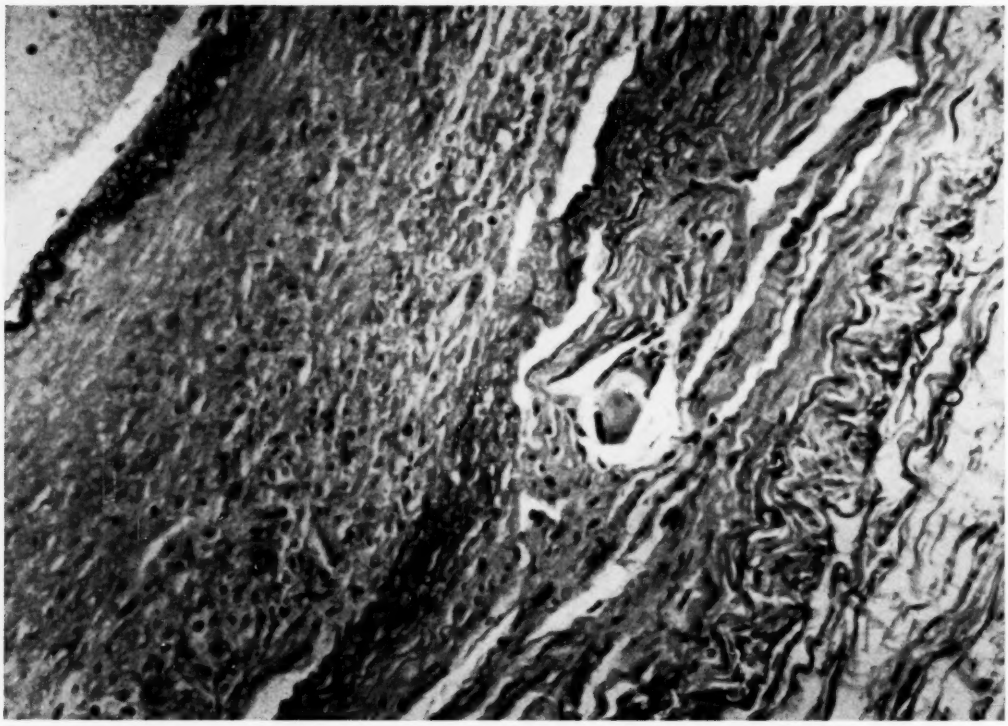


FIG. 6.—Temporal artery. Top left—lumen of artery. Next to this lies a broad fibrous band of thickened intima. The next layer shows disorganized, fibrotic media containing a giant cell. Adventitia lies to the right. (×374.)

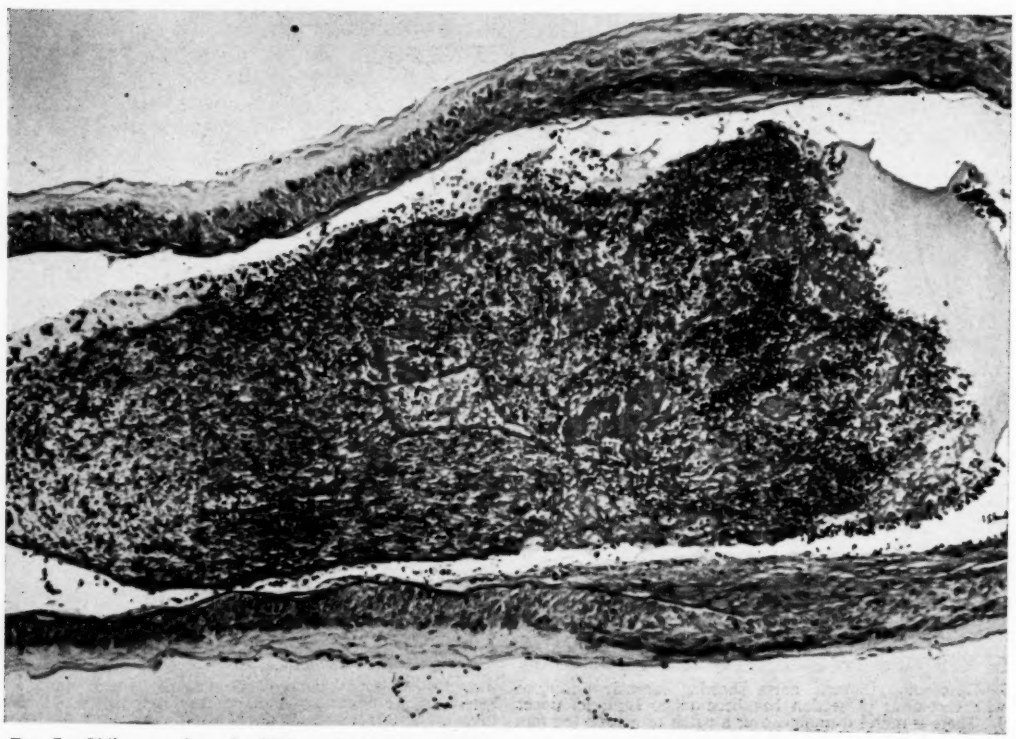


FIG. 7.—Oblique section of middle cerebral artery showing recent thrombus in lumen but no sign of arteritis. (×225.)

there was a mural thrombus (Figs. 4 and 5). At the diaphragmatic level was a flat film of thrombus apparently overlying aortic damage, and at various sites above this and in the carotid and subclavian arteries there was ill-defined scarring. Histologically the aorta showed severe scarring, more extensive than the macroscopic appearances suggested. The appearances were consistent with healed giant-cell arteritis. The *temporal arteries* did not show macroscopically recognizable lesions, but histologically showed typical changes of healed giant-cell arteritis (Fig. 6).

The *basal cerebral arteries* showed moderately severe atheroma. In the left middle cerebral artery, 25 mm. from its origin, at the point where it breaks into four branches, there was a fresh thrombus without any apparent arteritis. No arteritis was found histologically (Fig. 7). There was a fresh, slightly haemorrhagic infarct in the corresponding cerebral hemisphere, measuring 115 mm. antero-posteriorly and 45 mm. laterally, but without any softening. The infarct lay above the Sylvian fissure, reached to within 3 cm. of the vertex, within 20 mm. of the anterior pole, and ended posteriorly level with the end of the corpus callosum.

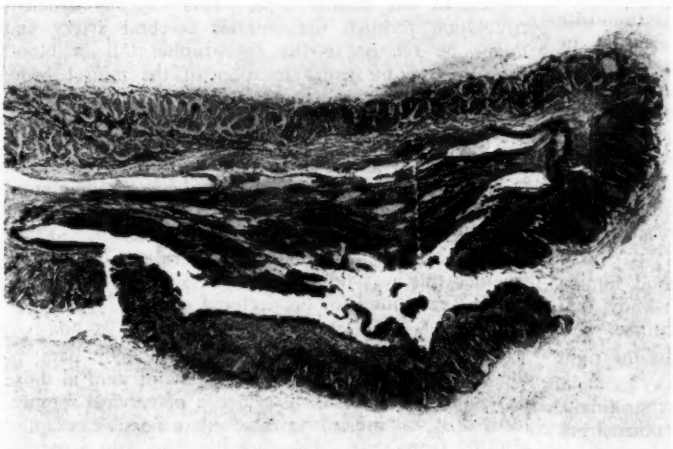


FIG. 8.—Renal vein occluded by old fibrous tissue and recanalized by numerous small channels. (×21.)

The *prostate* showed typical senile hypertrophy. The *bladder* was hypertrophied and dilated. Both *ureters* were a little dilated. The *right kidney* (202 g.) was hypertrophied and showed two small cysts and a little pelvic dilatation. The *left kidney* (68 g.) showed severe pyelonephritic scarring and organized thrombosis at the main renal vein (Fig. 8).

The *lungs* showed terminal bronchopneumonia and the *liver* showed signs of terminal cardiac failure.

Pathologist's Diagnosis

(1) Bronchopneumonia.

(2) Left ventricular hypertrophy and centrilobular congestion of the liver.

(3) Old giant-cell arteritis of temporal arteries and aorta.

(4) Cerebral infarction due to thrombosis of left middle cerebral artery (but no arteritis).

(5) Senile hypertrophy of prostate with mild dilatation of the bladder, ureters, and pelves.

(6) Pyelonephritic scarring of left kidney and organized thrombosis of main renal vein.

Discussion

Dr. COPE: There are two ways of looking at this problem. One is the general one of arteritis as a disorder, and the other is the specific problems that this individual presents. On the general point, he is a very good, indeed a typical, example of the so-called giant-cell arteritis. He shows very well the fact that what is called temporal arteritis is in fact a generalized disorder of arteries, and that you can divide up the symptomatology broadly into groups.

TYPICAL SYMPTOMS

First, there are the general disorders and manifestations, of which he showed all, I think: the loss of weight, fever, malaise, anaemia—these he had. Raised sedimentation rate and a leucocytosis he also had. Sweating and depression. All those things are characteristic of these people, but of course not specific. Secondly, there are the disorders referable to arteries which are likely to occur in many disorders. Myalgia is one; cerebrovascular accidents, of which he had one; coronary occlusion, which he apparently didn't have but which was suspected and which he might easily have had; abdominal artery thrombosis anywhere in the peritoneum, which was suspected once or twice; and intermittent claudication, which was a risk which he escaped.

Then there are the specific points, clinical ones, peculiar to this type of arteritis itself. A severe headache associated with temporal or occipital arteritis, often associated curiously enough with pain on chewing, which he didn't have. These patients are very seriously at risk through the ophthalmic artery for visual changes, which may include sudden, complete loss of sight in both eyes. At this age — the seventh decade — when temporal arteritis comes on so frequently, loss of sight is a major tragedy because the patient is at a stage when he can't learn to adapt to blindness easily. Briefly, the points of difference from polyarteritis or peri-arteritis are, first, that this has often a more benign course. It sounds rather absurd to say that in this case, but taking cases as a whole it tends to be true. There is less tendency to renal involvement. Peri-arteritis is likely to affect a younger age-group and it is much less likely—I should think practically never—to involve the aorta, whereas the so-called giant-cell arteritis not infrequently does.

MATTERS FOR SPECULATION

As points for discussion there are a lot of aspects specific to this man which one could raise; I had better raise only one or two at a time. I think there is no doubt that the pains in the shoulders and the back, at the time of his August, 1956, admission, were in fact multiple dissections and dilatations, referable to the aortic damage which occurred at that time, not to the myocardium. I am wondering whether you can tell us, or hazard a guess, as to how long the renal-vein thrombosis had been present, because there were several

occasions when he had sudden drops in blood pressure for various reasons. Another point on which somebody might like to speculate is why he had left ventricular failure in the presence of what looks to me like an awfully mild degree of myocardial fibrosis.

Professor HARRISON: The renal vein is completely fibrous: in other words, it has undergone all the organization it ever could. It occurs in the absence of any active inflammation, and all I can say is that it is old. I would say not less than six months, but, Heaven knows, it might be six years. With regard to the left ventricular failure, he had hypertension and he had hypertrophy, too. I would guess the weight of the heart as some 650 g. I can't give you the accurate weight because the aorta is still attached, but it is 750 g. with that bit of aorta, and I reckon there is probably around 700 g. of heart. I think the heart had every right to fail from hypertension in the presence of mild ischaemia. There is an account of an acute fatal dissection with sudden aortic rupture, due to giant-cell arteritis, by F. R. Magarey (*J. Path. Bact.*, 1950, **62**, 445); there is also one by G. C. McMillan of diffuse granulomatous aortitis—rather like this one (*Arch. Path.*, 1950, **49**, 63); and there is one by J. V. O. Reid (*Brit. Heart J.*, 1957, **19**, 206). There are hundreds of other references, but those refer specifically to aortic lesions in this disease.

Dr. COPE: You said, Professor Harrison, that the carotids had been involved, but was there any suggestion that their lumen had been blocked?

Professor HARRISON: No. They had good lumina up as far as the base of the skull. I don't know that we have information for the intraosseous course.

Dr. J. GOODWIN: Professor Harrison, was the right ventricle hypertrophied?

Professor HARRISON: It was, but not very strikingly. It is about 5 mm. thick in the conus: above normal but not exciting.

ROLE OF ANTICOAGULANT THERAPY

Dr. J. P. SHILLINGFORD: I see that in 1956 the treatment included anticoagulant therapy. Was this continued right through to 1959, and, if so, continued effectively? Do you think that it had any effect on the final result?

Dr. COPE: I think it was stopped as soon as the dilatation of the aorta was recognized. He certainly didn't have it beyond a few days.

Dr. SHILLINGFORD: In fact you would really say that this was a hazard of anticoagulant therapy, because it may have produced a haemorrhage.

Dr. COPE: One couldn't say it wasn't, I think. But you must remember that at that time we had an acute situation of a type which could occur again: severe pain, shock, suspicion of a myocardial infarct; plugging in of heparin (which is what he had straightway) and following up with phenindione; and then more leisurely assessment of the situation and I think quite sudden recognition (I was away when this happened) that the aorta had dilated.

FLUCTUATING BLOOD PRESSURE

Dr. SHILLINGFORD: There is something else which is very odd—namely, the fluctuation of blood pressure. It rises to 230/120, falls once more to 130/80, rises again to 245/140, falls again to 130/80 and then at the end it is down to 90/60, 80/55, and 100/70. Have you any explanation for this?

Dr. COPE: I have none at all. I haven't got an explanation for any kind of hypertension of this kind, I'm afraid. They were observed figures and nearly all confirmed by several readings. They are not random ones: one or two are but most of them are not. There is no doubt about these fluctuations.

Dr. GOODWIN: Could they possibly be related to his dissections?

Dr. COPE: I think they may have been. Some of them certainly were acute shock drops, but not all. The last one was terminal and is more easily explained.

NEUROLOGICAL COMPLICATIONS

Dr. C. PALLIS: There are two points of neurological interest. The first concerns the fact that the infarct extended well beyond the territory of the middle cerebral artery, affecting the most anterior and medial aspects of the frontal lobe. This suggests deficient circulation through the anterior cerebral artery and might be related to the catastrophic fall in blood pressure, the particular location of the infarct being determined by pre-existing stenotic changes in this particular artery. Was the lumen of the anterior cerebral of normal calibre? The second point concerns these pains at the back of the head in April, 1956. Occipital arteritis is common in patients with temporal arteritis. When elderly people start complaining of occipital headaches, the examination should always include palpation of the occipital arteries. I don't know whether this was done in this case or whether other causes were found for his occipital pain.

Dr. COPE: Actually I simplified this complicated story in the interests of time. He had pain in the back of the neck, which was a major item in those days, and there was *x*-ray evidence of cervical spondylosis, so it was difficult to dissociate a possible occipital arteritis from that. The fact that the pain went off later from the back of the neck and didn't recur is not necessarily in favour of its being occipital arteritis.

RADIOLOGICAL EVIDENCE OF AORTIC DILATATION

Dr. J. W. LAWS: I think the *x*-ray evidence of enlargement of the aorta (see Fig. 1) is interesting, because, if there hadn't been a normal film a month before, one would have been in doubt as to whether this was a recent enlargement or whether this was just the appearance of a man of 70 with an unfolded aorta anyhow. We attributed this to a dissection, and I should be interested to know, Professor Harrison, if there is evidence two and a half years later that the dissection has occurred from the root of the aorta right down to your shallow lesion at the diaphragm? Or are there just two isolated local areas of dissection, with no connexion between them?

Professor HARRISON: That is correct. As I said, it was unfortunate that I was unable to take low enough magnifications to show it in photomicrographs. They were two quite separate dissections.

Dr. LAWS: So after two and a half years you could recognize whether there had been a previous dissection?

Professor HARRISON: Oh, easily, because you stain the elastic tissues: if they have been torn apart, they stay apart. The other dissection was confined to the descending aorta. Both dissections were completely blind, but the distal one was filled with clot. There was absolutely no connexion between the two. Since we found severe, and I think widespread, medial destruction in the parts between these aneurysms, he

almost certainly suffered a diffuse enlargement of his aorta. I think it is only coincidence that your diagnosis of "dissecting" aneurysm instead of "dilating" aneurysm is correct.

When to Suspect Dissection

Dr. GOODWIN: One of the difficulties here, I think, and one which is not uncommon, is the fact that when you have hypertrophy of both ventricles the cardiographic diagnosis of infarction may be very difficult. It may be obscured, or it may be counterfeited. On looking through these tracings it is clear, as Dr. Cope has said, that this man never had unequivocal evidence of myocardial infarction. He undoubtedly had myocardial damage and biventricular hypertrophy. That is why I was interested in whether his right ventricle also was enlarged. I think a guiding principle upon which we should work is that, if somebody who is hypertensive has rather atypical chest pain, and a cardiogram which is not absolutely diagnostic of cardiac infarction, he may well have a dissection.

Dr. COPE: I think we ought to put on record the actual facts about the anticoagulant therapy. I see from the treatment sheets that he was given heparin for one day and part of the second day and then the treatment was cancelled. Two or three weeks later, he was again ordered heparin, presumably for one of these subsequent attacks, but it was deleted and not given. So in fact it was not more than a couple of days of anticoagulant therapy, but it might have been an aetiological factor nevertheless.

We are grateful to Dr. J. P. Shillingford and Dr. B. E. Heard for assistance in preparing this report, and to the photographic department of the Postgraduate Medical School for the illustrations.

JUST WHAT THE DOCTOR ORDERED

AN ANALYSIS OF TREATMENT IN A GENERAL PRACTICE

BY

RICHARD SCOTT, M.D., D.P.H.
Reader, General Practice Teaching Unit

J. A. D. ANDERSON, M.A., M.B., D.Obst.R.C.O.G.
Formerly Lecturer, General Practice Teaching Unit

AND

ANN CARTWRIGHT, B.Sc.
Lecturer, Department of Public Health and Social Medicine Edinburgh University

"Guérir quelquefois, soulager souvent, consoler toujours"—to cure sometimes, to relieve often, to comfort always—this concept of the physician's role, popular on the Continent a century ago, still has some relevance to-day. The fact that the doctor can now prescribe powerful and effective drugs that were not available a few years ago has not altered his basic functions, though it may have changed the relative emphasis which he places on these three broad therapeutic aims. Discussion of the present-day role of the general practitioner is hampered by lack of information about the range of therapeutic techniques which he commonly employs. Studies that have been carried out so far have tended to concentrate on such definable aspects of his work as prescribing,[1 2 3 4 5 6] the extent to which he is involved in certification,[4 5 7 8 9] the number and nature of the cases he refers to hospital,[7 8 11 12] and his diagnostic skills and ability.[10] Comparatively few facts are known, however, about the nature and extent of the social therapy dispensed by the general practitioner.

In this paper, which is based on a combined job analysis and morbidity study carried out over a period of one year in the Edinburgh University General Practice Teaching Unit, we have attempted to define and analyse the several components of the doctor's therapy. In this way the importance of such specific function as the prescribing of drugs, and the extent to which the doctor becomes involved in the social factors of the patient's environment, will be seen in perspective.

The work of the doctors in this unit is discussed with reference to prescribing, advising, explaining, discussing, listening, and treatment involving the use of the routine equipment of the consulting-room. The kind of work included in these categories is described and analysed, and the relevance of these findings to the concept of the family doctor's function is discussed. First we give a brief description of the ways in which the material was collected. The practice itself is then described, with particular reference to factors which are likely to influence the extent and nature of the doctor's work. This is followed by some comparisons with the results obtained in other studies of general practice. The pattern of morbidity encountered in this practice is then briefly described in order to provide a background for the main analysis of the doctor's treatment.

The Material

The study took place during the twelve months October 1, 1956, to September 30, 1957. During this period the doctors involved recorded details of all their consultations on a standard record sheet. (They completed these in addition to the clinical notes made routinely in the patients' files.) In this way information was obtained about the diagnostic and therapeutic action taken at each consultation. This information was pre-classified so that doctors knew precisely the alternative categories available and the amount of detail required. The classifications had been drawn up after various pilot studies and discussions with all the doctors involved. The doctor also recorded at least one diagnosis at each consultation. When he was dealing with more than one episode of illness at a single consultation* he recorded the action he took in respect of each diagnosis.

Most of this analysis of the doctor's treatment is in terms of the total number of consultations occurring during the year. Where this has been related to a specific disease, the relevant treatment given at all consultations for that disease has been considered. When the doctor modified his diagnosis during the course of an episode of illness the final diagnosis has been used in these analyses.

Information about the social circumstances of each patient and the household in which he lived was recorded in another file. These data were subsequently related to the consultations and to the episodes of illness in which the particular patients were involved.

The Practice

Edinburgh University General Practice Teaching Unit comprises two partnership practices with premises about half a mile apart in the centre of the city. Each practice is staffed by two doctors, a nurse, an almoner, and a

*This occurred at 7.2% of all the consultations.

secretary. The two practices are clinically independent, but for the purpose of this analysis they have been treated as a single unit, which is referred to as "the practice." All members of the staff are full-time employees of the University, and in addition to their routine clinical duties they are responsible for providing practical instruction for senior medical students.[13 14]

The number of patients registered with the practice is small in relation to the number of doctors involved. During the study-year the average number of registered patients was 4,805. If the small number of patients per doctor is to a certain extent offset by the teaching commitments of the doctors, the salient feature of this practice is that the family doctor has been replaced by a team comprising two general practitioners, a nurse, and a medical social worker. In this situation the doctor, nurse, and medical social worker are not acting as independent agents but as members of a team whose diagnostic and therapeutic activities are closely linked and co-ordinated. The nature of the work undertaken by the nurse and the social worker will be the subject of separate studies, but since it obviously has a direct bearing on the role of the doctors in this practice it is discussed in broad terms in this paper.

So far we have considered the organization and staffing of this practice, but, obviously, certain characteristics of the patients may also be relevant to the amount and nature of the type of work involved. The age distribution of the patients is shown in Table I, in which a comparison is made with the distribution in

TABLE I.—*Comparison of Age Distribution of Practice Population with that of Edinburgh and of Scotland*

Age Group (in years)	Practice Population	City of Edinburgh*	Scotland†
	%	%	%
Under 5	14·8	7·7	8·6
5–14	18·5	14·8	16·6
15–24	13·1	12·9	13·6
25–34	16·3	26·4	13·7
35–44	11·1		13·3
45–54	9·4	26·0	13·4
55–64	6·3		10·4
65 and over	10·2	12·2	10·4
Not known	0·3	—	—
Total population (=100%)	4,805	465,671	5,150,000

* Estimate from the Report of the Medical Officer of Health for 1957.
† Estimate from the Report of the Registrar-General for 1957.

Edinburgh and in Scotland. It will be seen that in this practice there is a relatively high proportion of children under 5 years of age and a dearth of people in the 45 to 64 age-group.

Housing conditions in this area in the centre of the city are poor and much lower than the average for Scotland or Edinburgh. Just over a quarter of the patients were living in households which contained more than two persons per room. Comparable proportions for Edinburgh and Scotland are 12% and 15% respectively, while in England the figure is 2%. In addition, a high proportion of the male patients were labourers and unskilled workers and there were relatively few non-manual workers.

Some Comparisons With Other Studies of General Practice

Under these conditions, in which this group of poorly housed patients has freedom of access to a partnership practice with the facilities of a nurse and a medical social worker, the average number of occasions on which patients saw the doctor during the study year was 6.6.† This is rather higher than the consultation rates reported in other studies of this kind. On the other hand, the prescribing rate was below the local and the national average, being 2.5 per patient in this practice during the study year, compared with slightly under 4 in the practice studied by Backett, Heady, and Evans,[4] 4.1 in that analysed by Brotherston *et al.*,[5] 3.8 for the City of Edinburgh, and 4.1 for Scotland.[6] The average cost per prescription was just slightly below the general average, but the cost of prescribing per patient at risk was appreciably below the average for the area.‡

TABLE II.—*Comparison of Proportion of Surgery Attendances, Home Visits, and Other Consultations in This and Other Practices*

Place	Our Practice	Practices Studied by General Register Office[2]	
		1952–3	1953–4
	%	%	%
Surgery, antenatal clinic, child welfare clinic	67·7	65·5	68·9
Patients' homes	20·7	28·6	26·8
Elsewhere	5·9	4·3	4·3
No. of consultations (=100%)	32,418	138,695	128,529

Other comparisons which it is possible to make with certain practices involve the ratio of home visits to surgery attendances and the issue of certificates. The proportion of consultations taking place in the patients' homes was very similar to that found in studies conducted by the General Register Office. Home visits accounted for 30% of all consultations in this practice, and 29% and 27% in the two studies covering 1952–3 and 1953–4 respectively (Table II). The number of certificates issued during the course of the study year was also very similar when expressed in terms of the average number per patient, but the proportion of consultations at which a certificate was written (13%) was considerably lower in this inquiry than in those undertaken by the General Register Office, in which it was 22% in 1952–3 and 20% in 1953–4.[7 8]

The relatively high consultation rate in this practice is clearly responsible for this last difference and may well affect various other aspects of the work undertaken by the doctors concerned. Before discussing the nature of this work in detail, we give a brief description of the patterns of morbidity presented, which it is hoped will put the ensuing discussion into perspective.

The Pattern of Morbidity

Of the consultations which took place during the year 76% were ascribed to one or other of the 25 diagnostic categories listed in Table III. This table also shows the number of episodes of each of these diseases and the number of consultations at which each diagnosis was recorded.

While the descriptive terms used for the episodes of illness shown in this Table are self-explanatory, two of the diagnostic categories—namely, "vague symptoms" and "social pathology" may require clarification. Vague symptoms comprise symptoms, senility, and ill-defined conditions—that is, Section XVI of the 6th International Statistical Classification 780–795 inclusive, with the exception of diarrhoea 785.6, enuresis 786.2, and observation without the need of medical care 793. Consultations for purely social misfortunes — for example, sudden death of a near relative, the committal of a husband to prison, the arrival in the household of an alcoholic grandmother, or the birth of a hydro-

†Based on the average registered population.
‡This information was extracted from data supplied by the local executive council to all doctors in the area based on the pricing of routine samples of National Health Service prescriptions.

TABLE III.—*Relative Frequency of the 25 Most Common Conditions*

Disease *	Episodes of Illness per 1,000 Registered Patients†	Consultations per Episode of Illness	No. of Episodes in Year	No. of Consultations in Year
Coryza, etc.	309·7	1·8	1,488	2,615
Superficial injuries	174·0	1·8	836	1,495
Vague symptoms	155·3	2·1	746	1,592
Sore throats	151·9	2·1	730	1,508
Skin sepsis	131·3	2·2	631	1,392
Child welfare, etc.	125·3	2·7	602	1,641
Exanthemata	102·4	2·8	492	1,396
Rheumatic diseases	65·3	3·8	314	1,181
Pregnancy	62·6	9·0	301	2,710
Otitis media	59·1	2·7	284	780
Styes and conjunctivitis	58·9	1·5	283	436
Diarrhoea (including dysentery)	53·1	2·4	255	607
Chronic bronchitis	49·9	5·7	240	1,364
Acute ,,	49·5	2·8	238	666
Dyspepsia, etc.	46·8	2·9	225	657
Cardiovascular degeneration	39·8	7·5	191	1,424
Asthma and allergies	37·7	3·1	181	562
Eczema	36·6	2·6	176	460
Psychoneurosis	36·4	4·4	175	771
Oral sepsis	34·8	1·8	167	306
Urinary infections	32·3	3·1	155	478
Chronic tonsillar hypertrophy	26·6	3·3	128	419
Social pathology	20·4	1·8	98	180
Pulmonary tuberculosis	17·7	6·4	85	545
Malignant disease	9·4	11·6	45	521
All other conditions	565·5	3·0	2,717	8,263
All conditions	2,452·2	2·9	11,783	33,969‡

Consultations with temporary patients are not included in this table.
* A detailed list of the diseases included under each heading may be obtained from the authors.
† Based on the average registered population.
‡ This is the total number of diagnoses made at consultations, and is greater than the total number of consultations.

cephalic child—where the symptoms of agitation, fear, or grief were regarded by the doctor as normal responses to the circumstances prevailing at the time, were classified under the heading social pathology.

Upper respiratory infection, minor trauma, skin sepsis, and symptom-complexes feature prominently as the commonest causes of morbidity. In this practice, which has a high birth rate and in which conditions are particularly favourable for the doctor who prefers to undertake personally antenatal care and child-welfare supervision, the exanthemata, pregnancy, and routine child welfare take up a substantial amount of the doctor's time.

Attention is drawn to the disparity between the prevalence of, and the consultation rates for, illnesses causing the bulk of the morbidity seen in general practice. Table III shows that while coryza, minor injuries, and septic skin conditions were responsible for a large number of episodes of illness with a low consultation rate per episode, pregnancy, degenerative cardiovascular disease, chronic bronchitis, pulmonary tuberculosis, and malignancy were outstanding in that, with a lower incidence, they gave a particularly high consultation rate per episode of illness. Psychoneurosis and rheumatic diseases also registered a consultation rate per episode that was substantially higher than average. In this paper we are in general limiting ourselves to an outline of a broad quantitative analysis of the doctor's therapeutic action without detailed reference to the patients themselves or the particular diseases with which they presented, but further analyses of the 25 conditions that accounted for the bulk of the consultations given during the year will be used to indicate, in general terms at least, the extent to which the patterns of therapy were conditioned by the kind of illnesses being treated.

The Broad Spectrum of Therapy

At any consultation the doctor could refer the patient to his nurse or to his social-worker colleague in the unit. This he did at 14% and 3% of consultations respectively. He could also obtain assistance from a medical or paramedical colleague outside the unit, and in fact sought such assistance at 3% of consultations.

Here, however, we are confining ourselves to a consideration of the treatment carried out by the doctor himself at the actual time of the consultation. Within the confines of the consulting-room or the patient's home, the forms of treatment which the family doctor provides fall into four broad groups. In the first instance he can give an injection, apply a dressing, syringe an ear, and take similar action which involves the use of his hands and the simple instruments available in the consulting-room or carried in his bag. Secondly, he can take out his fountain pen and write a prescription or complete a medical certificate. The third possibility is that of talking to the patient. Finally, as a form of therapy he can listen to whatever the patient wishes to tell him.

The proportions of consultations at which these various forms of action were taken are shown in Table IV. Talking to the patient emerged as the largest of the four main groups, with the use of the fountain pen a close second. When these were broken down a little further, prescribing was shown to be the most frequent single form of action, occurring at just under two-fifths of the consultations, while giving advice and explaining were each undertaken at about a quarter of all consultations. The nature of the therapy falling into these groups is now discussed in detail under the appropriate headings.

TABLE IV.—*Therapeutic Action Undertaken by Doctor*

Type of Action	Proportion of Consultations	
	%	
Direct action (dressings, injections, minor surgery, etc.)	10·8	
Prescriptions	37·8	47·5
Certificates	13·2	
Advice (diet, hygiene, smoking, etc.)	28·5	
Explanation (health and disease)	22·3	
Discussion about social services (including housing)	11·1	53·9
Discussion about work (job, housework, school)	3·9	
Discussion of personal relationships	3·2	
Therapeutic listening	3·4	
No. of consultations (=100%)	32,418	

Direct Action

The doctor performed some type of direct action in which he used his hands or his instruments at one out of every ten consultations. The most common form of direct action was the application of a dressing. This occurred at 8% of all consultations, while at 3% of consultations he gave an injection. Prophylactic injections were most frequently given at consultations for routine child-welfare supervision, while therapeutic injections were most commonly given for infections, cardiovascular disease, pulmonary disease, and malignancy. Minor surgery, including stitching, was undertaken on 330 occasions, which represent only 1% of all consultations.

Prescribing

At 38% of consultations the doctor wrote out a prescription for medicine and at 4% he handed out some medicine at the time of consultation. These figures, however, provide a somewhat incomplete account of the extent of medication, since at 17% of consultations the doctor told the patient to continue taking medicine which had been prescribed at a previous consultation. In addition, at 5% of the consultations he suggested that the patient should take some common

household remedy—such as an aspirin—but did not write out a prescription. This was normally either because small quantities were involved or because the doctor knew the patient already possessed the medicine. The suggestion in this last case came from the doctor, though occasionally, at 1.2% of consultations, the doctor encouraged the patient to continue with some form of self-medication which the patient had initiated. (Again the commonest example is aspirin and hot drinks for a simple respiratory infection.) Thus, at three-fifths of the consultations the patient was already taking medicine or was given a prescription or some suggestion about medication.

Rheumatic disease, asthma, eczema, and psychoneurosis, of the 25 common conditions, had the highest prescribing rates, while minor and superficial injuries and childhood disease were among the common diseases with a low prescribing rate per consultation.

Certificates

Certificates were given at 13% of all consultations during the year. Two-thirds of these were National Insurance certificates, and one out of every ten were other certificates relating to capacity for work which were required by the patient's employer. At 200 consultations (0.6%) during the year the doctor refused to grant the patient's request for a certificate.

Talking and Listening

Much has been written about the family doctor's role as guide, philosopher, and friend, and lip-service is often paid to the notion that he knows not only his patients and their physical infirmities but their psychological, spiritual, and social inadequacies as well. If this is so, one would expect that many consultations would include a substantial element of social exchange, the giving of advice, and the discussion of personal and social problems. We have examined four facets of this aspect of the doctor's therapy — namely, advice, explanation, discussion, and listening.

Advice and Instruction

The offering of unsolicited advice and instruction has long been accepted as part of the doctor's role in the orthodox management of disease. We should not, therefore, have been surprised to find that this form of treatment was given at as many as 28.5% of all consultations. The commonest form of advice and instruction was concerned with attempts to modify the patient's physical activities—for example, advice about going to bed earlier, resting, or rearranging the working day. The next most common form consisted of dietetic instruction and advice on nutrition in general. Then came a series of consultations where the doctor gave the patient routine advice or instruction on matters of personal hygiene—for example, menstruation, skin toilet, and oral hygiene. Finally, at a substantial number of consultations the doctor issued negative advice in the form of a number of prohibitions—not to smoke, not to drink to excess, not to take patent medicine, etc.

Table V shows the percentage of all consultations at which advice was given, and illustrates how the form of advice varied with the diagnosis in respect of five of the frequently encountered conditions. Rest was most frequently suggested for degenerative cardiovascular disease and pregnancy; dietary advice was also given relatively often for the former and most commonly for dyspepsia; advice on personal hygiene was given at a comparatively high proportion of consultations for eczema and skin sepsis. Patients suffering from eczema also came in for a substantial amount of prohibition.

TABLE V.—*Variation in Type of Advice Given with Nature of the Disease*

Nature of Advice	Consultations for: Degenerative Cardiovascular Disease	Pregnancy	Dyspepsia	Eczema	Skin Sepsis Other than Eczema	All Types of Disease
	%	%	%	%	%	%
Rest ..	26	28	9	3	4	14
Diet/nutrition ..	12	11	44	3	2	11
Personal hygiene	1	2	1	17	14	4
Prohibitions ..	4	4	5	13	5	4
All forms of advice	37	37	49	27	21	27
No. of consultations (=100%)..	1,424	2,710	657	460	1,392	33,969*

Consultations with temporary patients are not included in this Table.
* This is the total number of diagnoses made at consultations, and is greater than the number of consultations.

Explanation

Explaining as distinct from advising also featured as a frequent form of therapy, being provided at 22.3% of all consultations. Explanation about the normal healthy functioning of the body, simple psychology, or sex instruction was given at 4% of all consultations. Such explanation was most often given at consultations for pregnancy (26%) and at routine child-welfare examinations (11%). In contrast to this health instruction, explanation about the nature of the disease was given at 18% of all consultations. Explaining the nature of the illness was not recorded if the doctor merely told the patient the diagnosis in so many words. The giving of this form of treatment was recorded when the doctor was of the opinion that an adequate explanation of the nature of the disease and its implications for the patient had been given as a necessary part of the treatment—the patient needed this knowledge or insight in order to co-operate in the regime of treatment—or because he had certain misconceptions about the nature of the disease and its likely effects.

This heading therefore included those occasions when the explanation was directed at reassuring the patient that he did not in fact have some particularly sinister condition, where the doctor was explaining what the disease was not, or clearing up a misconception which the patient might have about the course or consequences of his illness. Here, again, while this kind of treatment was given at 18% of all consultations, the frequency with which such explanation was given varied particularly with the disease. Considering the 25 most common diseases, explanation was most often given to patients (or their relatives) at consultations for exanthemata (31%), allergic conditions (24%), or dyspepsia (23%).

Joint Discussion between Doctor and Patient

So far we have described therapeutic actions in which the doctor played a dominant role by giving advice, explanation, reassurance, or admonition. In the next section we discuss situations in which the doctor played an almost passive role, lending a sympathetic ear while the patient expounded on his fears and frustrations, doubts and dilemmas. There were yet other consultations at which both the doctor and the patient actively participated in a discussion. The three most frequent topics of discussion were the patient's social environment, his work, and his problems of personal relationships.

The patient's social environment, including the social and welfare services and the house in which he lived, was discussed at 11.1% of all consultations. At nearly half of these—5% of all consultations—the particular subject discussed was the hospital and specialist services. Here the doctor might be concerned with allaying the fears and anxieties which the patient had before admission to hospital, or the personal and family problems arising out of the hospitalization of the patient. Discussions about national insurance, pensions, local-authority services, legal aid, and voluntary social services were also included under this heading (Table VI).

TABLE VI.—*Variation in Discussion of Social Services and Housing with Nature of the Disease*

Subject of Discussion	Consultations for			
	Social Pathology	Pulmonary Tuberculosis	Pregnancy	All Types of Disease
	%	%	%	%
Hospital services	2	9	11	4
Housing	15	3	1	1
Ministry of Pensions and National Insurance	2	4	2	1
Ministry of Labour	5	4	—	—
Voluntary agencies	12	1	—	—
All social services	40	24		10
No. of consultations* (= 100%)	65	198	909	11,264

* Figures are for four months only and do not include consultations for temporary patients.

The patient's attitude towards work and problems of employment were discussed at 3.9% of all consultations. Again there was considerable variation with the nature of the illness. Consultations at which work and employment problems were often discussed were those for psychoneurosis 9%, eczema 7%, asthma 5%, and dyspepsia 5%, all of which are conditions that are often regarded as stress disorders.

Problems of personal relationship were discussed between doctor and patient at 3.2% of all consultations. During four months of the study-year the nature of the personal relationship problem was recorded in detail. For every 100 consultations at which personal relationships were discussed the nature of the relationships was compounded as follows:

Sexual relationship	16
Other marital relationships	33
Relationship to children on the part of parents	30
The patient's relationship to his or her parents	20
Other family relationships	14
Relationships outside the family	12

Among the 25 common conditions, the consultations at which personal relationships were most often discussed were those for social pathology 45%, psychoneurosis 17%, pulmonary tuberculosis 5%, and vague symptoms 5%.

Therapeutic Listening

On occasions in which this form of therapy was involved the doctor eschewed exhortation, the giving of gratuitous advice, and the two-way discussion, becoming in his attempt to "comfort always" a passive agent who merely listened. This form of treatment was recorded when the doctor allowed the patient to indulge in an emotional catharsis, when he lent to the patient a confessional ear or permitted the patient to engage in an emotional outburst. (We did not include here listening which was simply a part of history-taking.) The doctor gave this form of treatment at 3.4% of all consultations.

It seems that patients with intractable chronic conditions most frequently receive this type of treatment. A relatively high incidence of therapeutic listening was recorded for social pathology 33%, psychoneurosis 29%, vague symptoms 7%, rheumatism 6%, degenerative cardiovascular disease 5%, chronic bronchitis 5%, and malignant conditions 4%.

The Doctor's Auxiliaries

So far we have confined our attention to the nursing and social component of the doctor's treatment which was actually carried out by the doctor himself, but this account would be incomplete without some reference to the contribution made by the nurse and social worker as members of the family-doctor team. A brief account is therefore given of the degree to which the nursing and social elements of the doctor's therapy were extended by his referring the patient to one or both of these colleagues.

Of the patients who were registered throughout the whole year of the study, 72.9% were seen by the doctor, 28.9% were also seen by the nurse, and 17.6% by the medical social worker. The annual consultation rates per patient were as follows: with the doctor 5.97, the nurse 1.24, and the almoner 0.58.§

These figures, however, represent an understatement of the use which the doctor made of his paramedical colleagues, since there were opportunities at a daily case conference for discussing the patient or referring the patient informally to the nurse or to medical social-worker members of the team. In addition, regular and more formal conferences were held every three weeks throughout the year with health visitors, municipal midwives, and district nurses employed by the local health authority. Table VII lists five commonly prescribed items of treatment given both by the nurse and by the doctor, and illustrates the time-consuming forms of therapy performed by the nurse—namely, dressings, injections, dietary advice, explanation, and therapeutic listening. Similarly, Table VIII lists five of the topics of discussion common to both the doctor and the

TABLE VII.—*Comparison of Selected Items of Treatment Given Both by Doctor and by Nurse*

Treatment	Consultations with Doctor		Consultations with Nurse	
	No.	%	No.	%
Dressings	2,502	8	2,486	35
Injections	1,087	3	688	10
Diet advice	3,746	12	2,122	30
Explanation about disease	5,811	18	1,473	21
Therapeutic listening	1,113	3	1,549	22
No. of consultations (= 100%)	32,418		7,118	

TABLE VIII.—*Comparison of Discussion About Social Services and Relationship Problems by the Doctor and by the Medical Social Worker (Almoner)*

Subject of Discussion	Consultations with Doctor		Consultations with Almoner	
	No.	%	No.	%
Housing	131	1	489	17
Relationship problems	402	4	1,135	42
Ministry of Pensions and National Insurance	83	1	254	9
Hospital services	500	5	102	4
Attitude to work, employment, etc.	476	4	202	7
No. of consultations (= 100%)	10,678*		2,715	

* Based on data for four months only.

§Only patients who were registered with the practice throughout the study-year have been included here.

medical social worker. Here one notes that while the doctor does himself discuss with the patients relationship and attitude problems and the material circumstances of the patients' environment, it is in connexion with those particular aspects of the patients' social pathology that he is most likely to call on the services of the medical social worker.

Examinations and other Referrals

In so far as diagnostic procedures can themselves form part of the therapy, brief reference is made here to the doctor's diagnostic habits. The doctor himself performed some laboratory test, in the consulting-room, at 5% of all consultations, and sent off a specimen to a laboratory at 2.8% of all consultations. The patient was referred to open-access diagnostic *x*-ray services at 1.7% of all consultations, and at 3.1% of all consultations the opinion of a consultant colleague was sought. At 0.7% of all consultations the general practitioner sought and obtained direct admission to a hospital bed at the actual time of the consultation.

As a measure of the extent of the doctor's physical examination (Table IX) we find that the patient was undressed at 52% of all consultations. Undressing occurred most often at consultations for acute bronchitis 82%, exanthemata 76%, pregnancy 72%, and routine child welfare 64%, while only at 24% of all consultations for pulmonary tuberculosis and at 21% of all consultations for psychoneurosis was the patient undressed, though for each *episode* of these conditions the patient may well have been undressed on one or more occasions. The examination couch was used at 12% of all consultations in the consulting-room. Of the commonly occurring conditions, the couch in the surgery was most often used at consultations relating to pregnancy 65%, dyspepsia 24%, and urinary infections 23%. At 25% of all consultations there was no undressing or physical examination, and the doctor relied on history only.

Finally, and by way of summary, Table X lists the 25 most common diseases, which together accounted for 75.7% of all consultations between doctor and patient during the year; it also shows the frequency of prescribing, certification, advising, explaining, discussing, and listening which took place at consultations for each of these diseases. The Table also gives some indication of the doctor's diagnostic habits by showing for each disease the percentage of consultations at which there was no examination apart from history-taking. It also lists the percentage of consultations at which the doctor referred the patient to a specialist, and for each disease the frequency of his referral to the medical social (almoner) member of the family-doctor team.

TABLE IX.—*Doctors' Physical Examination of Patients*

Extent of Examination	Proportion of Consultations
Patient undressed	52%
Examination without any undressing	23%
History only	25%
No. of consultations (=100%)	32,418

Discussion

In general practice, as contrasted with specialist medical practice, the patient plays a much larger part in determining what kind of disease or what kind of clinical or social problem will be the initial subject of the consultation. This examination of the treatment given by the doctors in this practice provides some indication of the relative quantitative importance of the medical and social components of the work of the present-day family doctor. Though the prescribing rate in this practice was relatively low, medication is still one of the major forms of therapy, but providing explanation, advice, or information, discussing personal problems, and lending a sympathetic ear formed a very large part of the action undertaken by the patient's family doctor.

The significance of this recorded evidence of the doctor's preoccupation with the social and human relationship factors in the patient's environment raises important issues which are, however, beyond the scope of this article. For example, how do we assess the extent to which these personal problems are a function of the disease itself, or merely a characteristic of the patient as a person and unrelated to the disease for

TABLE X.—*Summary of Doctors' Therapeutic Action*

	Dressings	Injections	Prescriptions	Certificates*	Advice About: Rest	Advice About: Diet	Explanation (Health and Disease)	Social Services	Attitude to Work	Personal Relationships	Listening	History Only	First Referral to Consultant, Including Direct Admission	Referral to Almoner	Total Consultations in Year
	%	%	%	%	%	%	%	%	%	%	%	%	%	%	
Coryza, etc.	—	—	43	18	34	16	21	5	5	1	1	13	—	1	2,615
Superficial injuries	32	1	16	21	11	1	19	8	7	1	2	12	5	2	1,495
Vague symptoms	2	1	45	8	9	10	23	11	5	5	7	32	3	3	1,592
Sore throats	—	3	48	14	19	14	19	4	4	2	1	6	1	1	1,508
Skin sepsis	40	8	30	12	4	2	15	4	4	1	—	4	1	2	1,392
Child welfare, etc.	14	19	5	11	1	20	16	9	1	1	—	30	—	3	1,641
Exanthemata	1	1	24	8	24	13	32	3	2	1	—	12	2	1	1,396
Rheumatic diseases	3	1	62	13	9	7	12	12	4	3	6	37	1	3	1,181
Pregnancy	1	2	21	9	28	11	35	18	1	4	1	28	4	9	2,710
Otitis media	12	4	46	6	8	5	21	3	3	1	—	5	1	1	780
Styes and conjunctivitis	17	1	61	5	1	1	18	5	2	2	—	5	2	1	436
Diarrhoea (including dysentery)	—	—	45	14	12	40	19	8	3	—	1	42	4	1	607
Chronic bronchitis	—	5	50	13	16	8	13	10	3	2	5	37	2	3	1,364
Acute bronchitis	—	4	49	8	21	13	18	6	2	2	1	13	1	2	666
Dyspepsia, etc.	1	—	52	21	9	44	24	13	5	3	2	49	3	3	657
Cardiovascular degeneration	1	4	40	7	26	12	11	12	2	3	5	30	2	3	1,424
Asthma and allergies	1	4	62	15	6	8	25	5	5	2	1	37	1	3	562
Eczema	13	—	60	9	3	3	18	5	7	1	1	10	1	2	460
Psychoneurosis	1	—	60	13	4	8	26	13	9	17	29	66	2	7	771
Oral sepsis	4	10	25	12	4	2	22	17	2	1	2	17	2	1	306
Urinary infections	—	1	49	10	18	20	20	6	2	4	3	44	2	3	478
Chronic tonsillar hypertrophy	—	—	47	6	11	10	31	14	2	2	—	11	10	1	419
Social pathology	—	1	16	9	4	3	22	35	8	45	33	85	1	20	180
Pulmonary tuberculosis	1	3	39	33	6	4	11	23	5	5	3	74	3	5	545
Malignant disease	3	4	30	14	10	11	19	17	2	4	4	39	4	5	521
All types of disease	7	3	37	12	14	11	21	10	4	3	3	28	3	3	33,969†

* Based on figures for eight months only. † This is the number of diagnoses made at consultations, which is greater than the number of consultations.

which he is consulting his doctor ? To what extent does the recorded incidence of relationship problems vary not only with the disease and with the patient but with the individual doctor who sees that patient ? In so far as social therapy appears on occasion to be unrelated to the recorded clinical diagnosis, how far can an examination of the doctor's social therapy extend our knowledge of the incidence of minor neuroses and human relationship problems in general practice ?

What are the implications of these findings in relation to medical education? At present the clinical instruction of medical students is based almost exclusively on the hospital. Because of the need to ensure that the student is adequately informed about modern technical advances in therapy, and partly because of the nature of the clinical material which is available for instruction, the emphasis in teaching is almost inevitably placed on those aspects of therapy which are concerned with specific treatment of the definable major and specific clinical entities. In these circumstances, comparatively less emphasis can be placed on the complex problems of personal insecurity and social maladjustment which can loom so large in the daily work of the general practitioner. The newly qualified doctor entering this field equipped with techniques and attitudes acquired in the laboratory atmosphere of the teaching hospital may sometimes look askance at the idea that the patient may sometimes require pennies rather than penicillin, sympathy rather than surgery, or insight rather than an injection.

Though science has provided the modern family doctor with many more precise and specific cures in the form of powerful drugs which were denied to his predecessors, there is no evidence that proportionately less of his total therapeutic endeavour is concerned with the less tangible problems of fear, pain, personal insecurity, and social maladjustment. Because of the freedom of access to a personal medical attendant which has been granted to the whole nation by the provision of a National Health Service, the family doctor is more exposed than any other medically qualified person to a request for assistance with such problems. These requests occur frequently in the course of his routine daily work. The doctors working in this practice were certainly particularly concerned with the social and personal relationship factors in the patient's environment. Demonstrating the significance of these factors, both in the aetiology and in the treatment of disease, is a prominent feature of their teaching programme and one which is particularly appreciated by the students themselves.[15] This, together with the high consultation rate in this practice, suggests that a heightened awareness of the importance of these factors among family doctors in general would be likely to increase the demand for their services. This inference is supported by the findings of Mair and Mair.[16] From a study of their own general practice they conclude that efficient service to patients increases their demands and requires increasingly large expenditures of time and money.

The low prescribing rate found in our inquiry suggests that the increased cost of expanding our family doctor service might be partially offset by a reduction in the national drug bill. In this connexion, it is our impression that the nursing and social components of the problems which the patients themselves bring to the doctor are likely to be under-diagnosed and inadequately treated if the doctor is denied complete access to the services of a nurse and a medical social worker.

E

Summary

In the General Practice Teaching Unit of Edinburgh University some 5,000 patients receive family-doctor care under National Health Service conditions. The service available to the patients has been extended in quantity if not in quality in that the staffing of the unit is subsidized from university sources for teaching and research purposes. Doctors in this unit work in " family-doctor teams " comprising two doctors, a nurse, and a medical social worker.

A combined morbidity study and job analysis has been carried out in this practice over a period of one year.

The prescribing of drugs and the issuing of statutory certificates of incapacity for work were two of the major forms of therapy provided by the doctors.

Much of the family doctor's therapeutic endeavour, however, was concerned with the patient's social and personal circumstances and his psychological reactions to disease. In these circumstances, therapy took the form of giving advice and explanation, discussing with the patient his problems of adjustment to his disease, to the social and medical services which are available, and to the economic, social, and personal relationship factors which he encounters in the community and in the environment of his home.

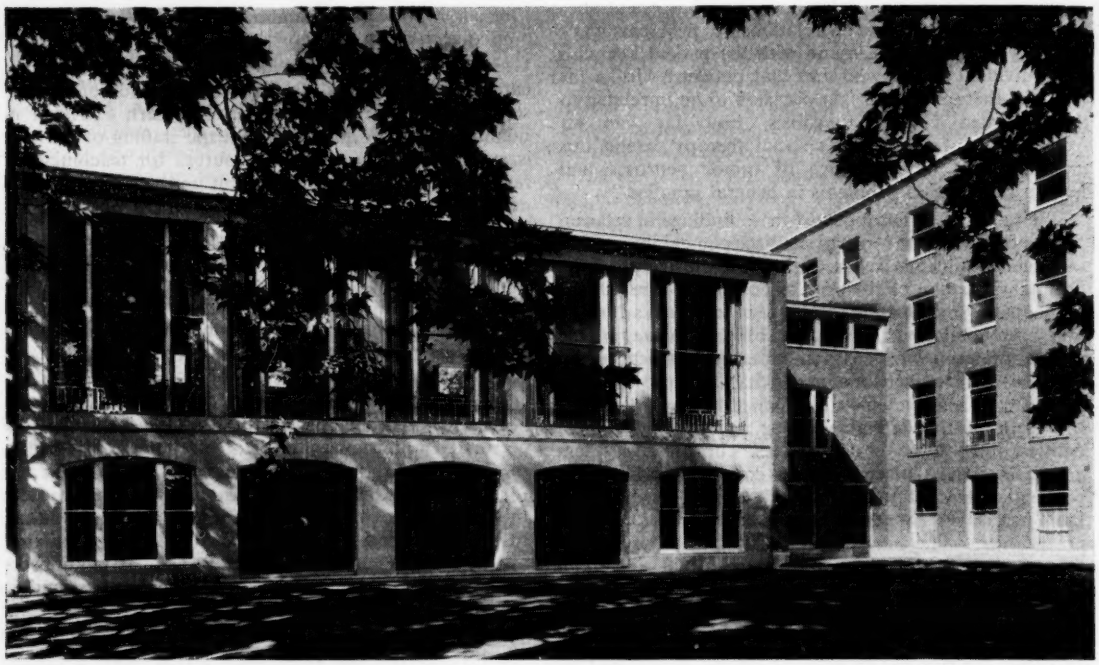
The relationship between the nature of the disease and the type of therapy prescribed is discussed in respect of a limited number of common conditions.

Results from the study reveal a relatively high consultation rate in the practice and a low prescribing rate. Possible reasons for this are discussed.

This preliminary account of a collaborative study would be incomplete if we did not record our indebtedness to the large number of individuals who made it possible. Our thanks are especially due to the patients of the practice. A good deal of extra clerical work was undertaken by our secretaries and in particular by Miss H. P. Pace. Mrs. N. Cheshire and Mrs. J. Gibson did most of the coding and transferred the data to punched cards. Mrs. E. Harnden was responsible for the tabulating and computing. Past and present members of the staff of the unit who assisted us in planning the study and in the actual collection of data included the following: nurses, M. J. Ferrier and J. Robertson ; almoners, J. McNicol, J. E. Paterson, and J. Throne ; doctors, D. W. MacLean, I. S. McRobbie, D. H. McVie, M. W. Moss, and H. R. Neve. The cost of the study was met by a grant made by the Secretary of State for Scotland on the recommendation of the Advisory Committee for Medical Research.

REFERENCES

1 Dunlop, D. M., Henderson, T. L., and Inch, R. S., *Brit. med. J.*, 1952, **1**, 292.
2 Martin, J. P., *Social Aspects of Prescribing*, 1957. Heinemann, London.
3 Ministry of Health, *Final Report of the Committee on Cost of Prescribing*, 1959. H.M.S.O., London.
4 Backett, E. M., Heady, J. A., and Evans, J. C. G., *Brit. med. J.*, 1954, **1**, 109.
5 Brotherston, J. H. F., Chave, S. P. W., and others, *Brit. J. prev. soc. Med.*, 1956, **10**, 200.
6 Department of Health for Scotland, *Scottish Health Statistics, 1958*, 1959. H.M.S.O., Edinburgh.
7 General Register Office, *Studies on Medical and Population Subjects*, 1956, No. 9. H.M.S.O., London.
8 —— Ibid., 1958, No. 14. H.M.S.O., London.
9 Pinsent, R. J. F. H., *Lancet*, 1950, **1**, 917.
10 Peterson, O. S., Andrews, L. P., Spain, R. S., and Greenberg, B. G., *Amer. J. med. Educ.*, 1956, **31**, No. 12, Part 2.
11 Hopkins, P., *Brit. med. J.*, 1956, **2**, 873.
12 Fry, J., ibid., 1959, **2**, 1322.
13 Scott, R., *Amer. J. med. Educ.*, 1956, **31**, 621.
14 —— *Res. Medica*, 1959, **1**, No. 4, p. 19.
15 Brotherston, J. H. F., Martin, F. M., and Scott, R., *Lancet*, 1959, **2**, 202.
16 Mair, A., and Mair, G. B., *Brit. med. J.*, 1959, **1**, Suppl. p. 281.



[Colin Westwood, Weybridge

FIG. 1.—New home of the Royal College of Obstetricians and Gynaecologists in Regent's Park.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

NEW BUILDING OPENED BY THE QUEEN

On July 13 HER MAJESTY THE QUEEN opened the new building for the Royal College of Obstetricians and Gynaecologists in Sussex Place, Regent's Park, less than three years after the laying of its foundation stone by the Queen Mother.[1] The college was designed by the London firm of architects, Messrs. Louis de Soissons, Peacock, Hodges, and Robertson, and was built by Messrs. J. Gerrard and Sons Ltd., of Manchester. It cost about £400,000, of which £125,000 was provided by Lord Nuffield and the Nuffield Provincial Hospitals Trust, £30,000 each by the Wellcome Trust and the College's own fellows and members, and £10,000 each by Lord Riddell and the Simon Marks Trust. Both the foundation and the opening have fallen within the same presidency of the College, that of Sir ANDREW CLAYE.

Opening Ceremony

Inviting the Queen to declare the College open, Sir ANDREW said that for many of them this was a day of memories. He had particularly in mind December 5, 1932, when the Queen's father and mother, then Duke and Duchess of York, had opened the Florence Blair-Bell House at 58, Queen Anne Street, given to them by their first president, William Blair-Bell; when the College, from being a small body of men and women, became also the geographical home of British gynaecology. Some of the audience had been present then, when Blair-Bell and his honorary secretary, William Fletcher Shaw, supported by the leading gynaecologists of the British Isles and of the Commonwealth, passed that important milestone on the way towards the realization of their ideals.

They were specially happy, continued Sir Andrew, that the Queen's opening of this college fell in the year of the birth of Prince Andrew, whose progress they were following with the lively attention common to all her loyal subjects, heightened by the special interest they felt in their most distinguished Fellow's new baby. "Let us then continue our forward march, warmed and heartened by Your Majesty's presence here to-day, by the presence of many colleagues

[Sunday Times

FIG. 2.—The Queen, accompanied by Sir Andrew Claye, P.R.C.O.G., unveiling the commemorative plaque at the entrance of the new building.

[1] *Brit. med. J.*, 1957, **2**, 1170.

[Colin Westwood, Weybridge

FIG. 3.—The council chamber.

and friends, and better placed physically than ever before. May this college building be the outward and visible sign of an inward and spiritual urge that will continue to generate advances in obstetrics and gynaecology throughout the British Commonwealth."

Sir Andrew then called upon the Queen to formally declare the College open, and to address them.

In her reply, THE QUEEN recalled her honorary fellowship of the College nine years ago. "I have always been proud of my honorary fellowship," she said, "and it is a happy chance for me that the opening of your new building gives me the opportunity of expressing my personal thanks to those of your great fraternity to whom I owe so much." Expectant mothers could now look forward calmly and confidently to the birth of their babies. "Indeed," she added, "you have given almost literal meaning to Wordsworth's assertion that 'our birth is but a sleep and a forgetting.'"

Sir JOHN PEEL, honorary treasurer of the College, then thanked the Queen and presented her with a specially bound copy of *The Oxford Dictionary of Nursery Rhymes* and a copy of *The Oxford Book of Nursery Rhymes* for Prince Andrew.

After touring the building, the Queen unveiled the tablet at the entrance which commemorates the opening ceremony (Fig. 2).

The New Building

The brick and Portland stone building occupies a triangular site, the frontage facing the lake in the outer circle of Regent's Park, and bounded by Park Road and Kent Passage. It is designed exteriorly to conform to the Nash terraces. One section of the building is occupied by the Academic Wing, the other by the Administrative Block and members' rooms.

Academic Wing

Entrance.—On the right side of the porch is the foundation stone laid by Her Majesty Queen Elizabeth the Queen Mother. On the left is the stone commemorating the opening by Her Majesty the Queen. In the entrance hall, lined with Italian marble, is a plaque bearing sculptures in bronze of William Blair-Bell and William Fletcher Shaw. The inscription reads "William Blair-Bell, William Fletcher Shaw, by whose inspiration, vision, and determination this College was founded in 1929."

Library.—The Library is lined with open shelves and panelled in elm. Recesses at the ends are occupied by two bookcases, one Chippendale, one early Georgian, bequeathed by Professor William Blair-Bell. These closed bookcases house the old historical books. The readers' tables and chairs and the librarian's desk are in beech. There is an office adjacent to the library.

Wellcome Research Museum. — The pathological museum comprises ten "bays" lined with shelves; a large bay at the end is available for demonstrations. Special attention has been given to the lighting. The case in the centre isle houses a collection of Chamberlen forceps and other relics of the Chamberlen brothers. The arrangement of the museum is such that it provides accommodation for the examinations of the College. The main staircase leading to the first floor is lined with elm veneer.

Nuffield Assembly Hall.—The hall is panelled in African walnut and marble; a portrait of Lord Nuffield is recessed on the right; the coat of arms is incorporated in the carpet. The large windows occupying the entire left side command a magnificent view of the park and lake. As the hall is to be used primarily for lectures and conferences, full projection equipment has been installed. The screen for it is concealed behind a sliding panel in the back of the platform; the decorative ceiling incorporates a lighting system which meets the requirements for films. There are 230 chairs in walnut, each with a commemorative name carved on the back.

Council Room Suite.—This comprises a committee room, the council chamber (Fig. 3), and the robing room. Folding doors divide the two main rooms. The council furniture is that from Queen Anne Street augmented by new tables. The coat of arms of the College is incorporated in a stained glass window (Fig. 4) behind the president's chair.

Administrative and Members' Block

Off the ground-floor corridor is the suite of offices which will be used for the College's administration. There are

[Nursing Mirror

FIG. 4.—The coat of arms in the stained glass window in the council chamber.

also staff cloakrooms and a kitchen. The president's office is on the first floor and is furnished from the bequest of William Blair-Bell. The secretary's and assistant secretary's offices are on the same floor. On the second floor there is accommodation for members, consisting of changing and toilet rooms, common rooms, and a writing room. There is also a large committee room which may be used as a council dining room.

The week's celebrations ended with a banquet at Guildhall, at which the Lord Mayor, Sir Edmund Stockdale, responded to the President's toast "the Lord Mayor, the Corporation of London, and the Sheriffs."

MEDICAL RESEARCH COUNCIL ANNUAL REPORT FOR 1958–9

[FROM A SPECIAL CORRESPONDENT]

The annual report of the Medical Research Council for the year ended September 30, 1959, has just been published.* This, the 45th, is a lengthy document, consisting of three main sections, devoted to policy and administration, some aspects of research, and details of the work done by units controlled or assisted by the M.R.C. Some important recommendations are made for future policy.

Important Policy Changes

The Council, while recognizing the value of maintaining individual units, feels that the time has come to establish a Clinical Research Centre "comprising a comprehensive concentration of relevant clinical and paraclinical disciplines," which would be the equivalent in the clinical field of the National Institute for Medical Research at Mill Hill. This would allow for the planning of collaborative work, which is at present impossible under the system of establishing M.R.C. Units in individual hospitals or university departments. It is proposed to house the new Centre in an existing general hospital, since it is felt that a separate hospital for research purposes would be inappropriate in this country.

The Council has also reviewed the present arrangements for sponsoring research in tropical medicine in the light of the rapidly changing political situations of Colonial and Commonwealth countries. The value of research in this field not only to the country concerned but also to the United Kingdom and the importance of ensuring adequate recruitment of medical personnel are stressed. A new Tropical Medicine Research Board is to be set up not only to take responsibility for prosecuting research, but also to implement recommendations set out in the report for safeguarding individuals who may wish to take up this work.

Finally, the Council turn to the question of psychiatric research, in which it has already taken considerable interest. In addition to the four units which are in existence, two new units have been established—one on psychiatric genetics (Maudsley Hospital) and one on the epidemiology of mental disorders (University College Hospital). Committees dealing with clinical psychiatry under the chairmanship of Sir George Pickering and the epidemiology of mental disorder under Sir Aubrey Lewis have also been set up. Career prospects in psychiatric research are considered to be good, and the new Mental Health Act, 1959, should help to attract suitably qualified scientists and doctors to this expanding field.

Budget of £3,500,000

During the financial year covered by the report Parliament provided the Council with just under £3,500,000, an increase of about £400,000 on the previous year. Establishments supported consisted of the National Institute for Medical Research, the M.R.C. Laboratories in the Gambia, and 71 research units. The Council also assisted numerous individuals as members of its external staff and with grants and training awards, and provided block-grants for the Institute of Cancer Research, London, the research department of the Royal Beatson Memorial Hospital, Glasgow, the research programme of the Christie Hospital and Holt Radium Institute, Manchester, and of the Strangeways Research Laboratory, Cambridge. The Public Health Laboratory Service and the Blood Products Laboratory (Lister Institute) were administered by the M.R.C. on behalf of the Ministry of Health, but the present report records that the P.H.L.S. is to be administered in future by a separate P.H.L.S. Board.

In addition to the psychiatric research units already mentioned, six new units have been set up during the year. These are the Blood Coagulation Research Unit (Dr. R. G. Macfarlane) and the Bone-seeking Isotopes Research Unit (Dame Janet Vaughan), both at Oxford, units for research in mutagenesis (Dr. Charlotte Auerbach) and environmental radiation (Professor F. W. Spiers) at Edinburgh and Leeds respectively, an Experimental Virus Research Unit at Glasgow under Professor M. G. P. Stoker, and a Rheumatism Research Unit at Bath under an honorary board. The total number of scientific and medical staff employed by the Council numbered 709, with an additional 153 in the P.H.L.S.

ASPECTS OF MEDICAL RESEARCH

Occupation and Coronary Heart Disease

The M.R.C. Social Medicine Research Unit has been a pioneer in epidemiological studies of coronary heart disease. Studies of busmen and post-office workers have established a higher incidence of severe coronary disease among those with light or sedentary occupations. Complementary E.C.G. and post-mortem investigations have confirmed that the more serious lesions tend to occur in those with the lighter occupations. Nevertheless there are still unexplained differences in frequency within the various grades of "light" work. For instance, general practitioners are more prone to serious coronary disease than other classes of doctor; there is a high mortality among radio and telegraph operators; and the incidence among leading Government officials is low. The latter observation is perhaps a further blow to the importance once attached to nervous factors. At any rate the relationship to occupation has led to a revaluation of the effect of exercise on blood flow and clotting. It is probable that regular exercise enlarges the anastomoses between the two coronary arteries, besides tending to lower blood lipids, to slow down clotting, and to increase fibrinolysis. Blood lipids tended on the whole to be higher among bus drivers than among conductors, and a field study is at present in progress among workers at H.M. Dockyard, Portsmouth, to determine the relation between clotting and various occupations. The increased incidence of coronary artery disease may reflect the increasingly sedentary nature of work, transportation, and leisure, and as the working day becomes shorter the uses to which leisure is put assume added importance.

Chemotherapy of Tuberculosis

With the control of malaria, tuberculosis is now the world's most important communicable disease, and it is estimated that there are between 1½–2½ million infectious cases in India alone. In underdeveloped countries the need is for a cheap drug, which is easy to administer and effective for domiciliary treatment. Isoniazid fulfils these requirements, but the development of resistant organisms requires that it should not be given as the sole treatment. M.R.C. Units working with hospitals and laboratories in East Africa have shown in carefully controlled clinical trials there that the response to combined treatment is as satisfactory as that obtained in Britain. A search is now in progress for a drug comparable to P.A.S. in its ability to prevent the emergence

*Cmnd. 1082, 1960. H.M.S.O., London (price 15s. 6d. net).

of resistant organisms. Diamidodiphenyl sulphone (D.D.S.), used in the treatment of leprosy, was found to be unsatisfactory, but thiosemicarbazone thiacetazone, originally developed in Germany as an anti-tuberculous agent but discarded as too toxic in the doses used, is more promising. Combined with isoniazid it can be given in smaller dosage and is moreover acceptable and cheap. An unexpected rise in the incidence of initial drug-resistance in patients in East Africa underlines the need for adequate treatment.

In India, M.R.C. Units in co-operation with local research workers have compared the response to treatment with isoniazid and P.A.S. of 100 patients treated in hospital with a similar number treated at home. The results after a year were similar and satisfactory, and rather surprisingly factors such as poor diet, poor housing, little rest or nursing care, and irregularity in medicine-taking, usually regarded as adverse, had little harmful effect. The risk to contacts of those treated at home was found to be relatively high, especially among the young, during the initial period of treatment, but was very rapidly reduced. The co-operation of patients was especially gratifying in these studies, which were carried out in conjunction with the Governments concerned and with interested bodies such as W.H.O.

Clean Air in Operating Theatres

Investigation of hospital outbreaks of *Staph. aureus* infection have shown that operating theatres may provide a potent source of cross-infection. This can be mitigated to some extent by attention to the clothing worn by staff, the exclusion of contaminated bedding, the detection of carriers, and the restriction of movement in the theatre. Even so a proportion of pathogenic organisms remain in the air, and it is the function of the ventilating system to remove these as rapidly as possible. Efficient ventilation depends on exclusion of air from other parts of the hospital and on the maintenance of positive pressure to ensure an outward flow of air at all times. Ideally exhaust fans and ports should be dispensed with entirely, and the air allowed to find its way out through natural openings. In a well-built theatre, however, this may not be practical, and a simple solution is to provide exhaust ports fitted with weighted flaps, which close when doors are opened, sited in positions to ensure the desired pattern of airflow. The best method of supplying air is believed to be by a series of symmetrical inlets in the ceiling. In order to displace contaminated air in the theatre the incoming air must be a few degrees warmer than the room temperature.

Various methods of ventilation have been tested in dummy theatres using culture plates and gaseous materials such as acetone and nitrous oxide to determine the "dynamics" of contamination. Important practical points which emerge are that in twin theatres the amount of contamination in the second theatre may be as much as a quarter that of the air in the one in which the organisms were liberated; and that where autoclaves are installed very careful attention must be given to thermal insulation, otherwise the heat generated will effectively defeat the whole purpose of controlled ventilation. Important as these experimental studies are it remains to be seen whether they hold good for a theatre under normal working conditions. The difficulty of obtaining reliable information in such circumstances is outweighed by the practical advantages which may be expected.

Genetics and Chromosomes

Accumulation of data on human genetics is hindered by such factors as the long interval between generations, the need to rely on observation rather than experiment, and the difficulty of distinguishing between hereditary and environmental influences. Nevertheless, methods for the measurement of mutation rates have been devised for man, and estimates of spontaneous mutation rates are now available for about fifteen harmful but uncommon dominant and for three sex-linked recessive traits. Similarly the relative importance of environmental and genetical factors in the production of congenital malformations is gradually being elucidated. Associations with consanguinity, intrauterine environment, hydramnios, twin pregnancies, and familial incidence have been noted for certain malformations, as well as seasonal, geographical, and social trends. The value of a knowledge of specific characteristics of large human populations is illustrated by the discovery of an association between blood groups and certain diseases. Three such associations have been definitely established: group A and cancer of the stomach, group O and non-secretors of ABO antigens with duodenal ulcer, and group A with pernicious anaemia. It is possible that rheumatic fever, diabetes mellitus, and thyroid disorders may be correlated respectively with non-secretors, group A, and ability to taste phenylthiocarbamide.

Two of the most spectacular advances in genetics have been the discovery of the chromatin body in the tissue cells of females and the development of techniques for studying chromosomes in bone-marrow cells, skin, and leucocytes. The presence of sex chromatin indicates a female sex-chromosome constitution (XX) and its absence a male sex-chromosome constitution (XY), except in certain developmental abnormalities where the sex phenotype is at variance with the sex chromatin, namely Klinefelter's and Turner's syndromes and testicular feminization. Chromosome counts have now established that the normal number in man is 46 and not 48 as previously supposed; this is made up of 22 pairs of autosomes and a pair of sex chromosomes. Autosomal abnormalities have been found in mongols, who have an extra chromosome indistinguishable from a member of one of the smallest pairs: they are thus said to be trisomic for this particular autosome. A number of other isolated examples have been found in patients with multiple congenital defects. Abnormalities in the sex chromosome occur in Klinefelter's syndrome, where the total is 47 and the sex chromosome XXY, and in patients with Turner's syndrome who have 45 chromosomes and a constitution XO. A "super female" has been described with 47 chromosomes and sex chromosomes XXX. Other interesting phenomena are being uncovered, including "mosaics" in which bone-marrow cells contain two different complements of chromosomes, and abnormalities in some patients with leukaemia. There is little doubt that we may expect further advances in this field not only in relation to specific diseases but also in the wider view of population genetics.

Structure of Viruses and Muscle

Electron microscopy and *x*-ray crystallography have confirmed mathematical predictions that the protein coat of a virus is built up of a number of small sub-units rather than in the form of a giant protein. This varies from 60 in the case of small spherical viruses to over 2,000 in those with a helical structure like the tobacco-mosaic virus. In the case of smaller particles it is relatively simple to predict how the sub-units will be arranged—indeed, this was done by Plato for spherical objects—but the more complex patterns can only be worked out with the aid of modern techniques. The adenoviruses, for example, of which 18 different types are known, have been shown to be icosahedra, structures with a regular surface made up of 20 equilateral triangles. Each edge is composed of six molecules, and there are 252 sub-units in all. The bacteriophage T_2 is even more complex and appears to be shaped like a tadpole. Every part of the structure, however, probably depends on geometrical laws for its shape, and this must be brought about by folding of the polypeptides and nucleotides which make up the virus.

Similar studies in muscle have led to the abandonment of the theory that contraction is due to a change in the manner of folding of the polypeptide chains of actomyosin. *X*-ray diffraction techniques failed to reveal any change in pattern on contraction, while electron microscopy showed that the myofibril consisted of a double layer of thick (myosin) and

thin (actin) filaments linked by bridges—the cross striations—which probably represent actomyosin formation mediated in turn by adenosine triphosphate. On contraction both types of filament maintain their length but move relative to one another by a so-called *sliding filament mechanism* produced by changes in length of the sarcomere. The mechanism is extremely complex, but appears to be present in both striated and smooth muscle.

Returning to viruses, epidemiological studies have shown that those viruses which require a period of growth in an insect host, the "arbor" viruses, can be divided into three major groups, designated A, B, and C. Since 116 are already known this step is likely to lead to considerable simplification. Group B contains the organisms of yellow fever, dengue, the various forms of encephalitis, and louping-ill, the only arbor virus which occurs in this country. It is highly probable that the groups contain shared antigens and that cross immunity may arise as a result. This would explain the relative tolerance of native populations to yellow fever, as well as the geographical zoning of some of the diseases in spite of suitable insect vectors.

Interferon; Kinins; and Inattention

There is a progress report on interferon, the anti-viral agent which was discovered three years ago by workers at the National Institute for Medical Research. Toxicity studies in animals are encouraging so far, and although the substance is a protein the search for antigenicity has been negative. One important practical point is that interferon must be prepared in cells of the species of animal it is intended to protect, because of a certain tissue-specificity. Another is that in order to have most effect it must be given at an early stage of infection—i.e., in the incubation period—and in mammals will probably have to be administered daily. Its action appears to be on infected cells, possibly by shifting the metabolism of substances like glucose away from the virus and towards the cell. The question of large-scale manufacture is still being pursued, but results are encouraging. Interferon protects against a variety of viruses, so that it is to be hoped that technical problems in production will soon be overcome.

The plasma kinins are a group of polypeptides with vasodilator properties formed from plasma proteins by the action of proteolytic enzymes. Although they have been given different names (bradykinin, kallidin, etc.), according to the method of preparation, it is possible that they may be one and the same substance. They have a stimulant action on smooth muscle, cause vasodilatation of peripheral arterioles, increase permeability of blood vessels, and are associated with the vasodilatation that accompanies salivation and sweating. They are capable of causing severe pain, and there is speculation as to whether they may be mediators of the inflammatory response. Bradykinin, for instance, is more active than acetylcholine or histamine. It has been purified and shown to be an octapeptide; synthesis of a molecule of this size is a practical proposition, and we are likely to hear more of the kinins in the future.

Finally there is the important practical problem of inattention and its relation to accidents. The application of communication theory has been of great value in showing that the central nervous system is analogous to a single channel of limited capacity; it does not act as a receiver of an unlimited number of independent stimuli. Thus in the same way that a telephone system cannot transmit a message if its channels are already fully occupied, so the brain may be unable to respond to a stimulus, *even though a clear signal is received.* The speed of reaction depends not only on the number of stimuli, their variety and predictability, but also on learning and on personal factors. Thus distraction may be brought about if the sources of information are too numerous (and especially if simultaneous) or if excessive stimulation—for example, by noise—occupies too much of the channel. The effects of fatigue in causing errors set in early—after half an hour—if subjects are expected to spot signals during long periods of inactivity, in radar for example. Furthermore, unexpected messages are poorly dealt with, the time taken in transmission being inversely related to the probability of the message being sent. In addition to "environmental" factors of this sort there are also temporary changes in "capacity" of the nervous system itself. These depend on the reticular activating system, which acts in parallel with the direct sensory pathways to the cortex, so that all incoming stimuli provide a widespread alerting discharge throughout the brain. The need for general stimulation of this sort is strikingly illustrated by experiments in sensory deprivation, in which subjects deprived of the normal contacts provided by sound, vision, and touch, rapidly lose their ability to respond to other stimuli and soon become dangerously hallucinated.

Nova et Vetera

THOMAS ADDISON

1793–1860

Thomas Addison, who was born at Long Benton, near Newcastle, in April, 1793, was descended from a family of Cumberland yeomen. He was educated at Newcastle Grammar School and the University of Edinburgh, where he graduated M.D. in 1815 with an inaugural dissertation entitled "De Syphilide et Hydrargyro." He came to London, where for a time he was house-surgeon to the Lock Hospital and physician to the Carey Street Dispensary. In 1817 he became a "perpetual Physician's pupil" at Guy's, where he attracted the favourable notice of the all-powerful hospital treasurer, Benjamin Harrison, junior. In 1824 he was appointed assistant physician to the hospital, in 1827 lecturer on materia medica, and finally, in 1837, physician and joint lecturer on medicine with Richard Bright.

The story of Addison's life is inseparably linked with Guy's. His private practice remained small and his whole professional interest was centred on the hospital, where his brilliance for clinical teaching and research was soon established. Together with Bright, William Gull, Samuel Wilks, and Thomas Hodgkin, Addison was responsible for the high reputation that Guy's enjoyed in the mid-nineteenth century. He remained senior physician until shortly before his death on June 29, 1860. He is buried at Lanercost Abbey, in Cumberland.

Outwardly a proud and haughty man, Addison was in reality a nervous and timid character. His pupils have testified to his discomfiture at the beginning of every lecture. He was slow to publish the results of his research, but his sparse scientific papers are rich in original contributions to medicine and reveal the diversity of his interests. In 1829 he collaborated with John Morgan, a colleague at Guy's, in the first book in English on the actions of poisons on the living body. In 1837 he was the first to advocate the use of static electricity in the treatment of certain spastic disorders. The first volume of a textbook of medicine which he published with Richard Bright in 1839 contains the earliest accurate account of appendicitis.

Dermatology and the study of chest diseases were both fields in which Addison achieved distinction. An interest in skin diseases dated from his early days in London, when he had studied under Thomas Bateman. He founded the skin department at Guy's and was responsible for the very fine collection of wax models depicting diseases of the skin still to be found there. In 1851, together with William Gull, he published a classical account of xanthoma multiplex. But Addison's main interest throughout his life were diseases of the chest. His tireless research into morbid anatomy enabled him to refute the belief that the so-called "parenchyma" of the lung was the site of pneumonia and to establish that the disease was in fact inflammation of the air cells. He showed also that the symptoms of "phthisis" could be caused by diseases other than tuberculosis.[1]

Addison is best known to-day for the two diseases which bear his name, pernicious anaemia or Addison's anaemia, and adrenocortical deficiency or Addison's disease. In 1849, in a paper to the South London Medical Society entitled "Anaemia-Disease of the Supra-renal Capsules," he provided an accurate clinical picture of pernicious anaemia. His claim to have discovered the condition is disputed by James Combe, of Leith, who had reported a case of severe anaemia in 1824, but it was Addison who succeeded in bringing the disease to the notice of the medical profession. In this article he revealed his growing interest in the suprarenal capsules. The adrenals were first described by Eustachius, whose work was published in 1714, but their function was so badly understood in the eighteenth century that, when the Académie des Sciences of Bordeaux offered a prize for an essay on their use, no entry was received worthy of the award. This ignorance continued into the nineteenth century until in 1855 Addison published his finely illustrated monograph entitled *On the Constitutional and Local Effects of Disease of the Supra-Renal Capsules.* The salient features of adrenocortical deficiency were vividly described, and the work stimulated C. E. Brown-Séquard to prove by the experimental removal of the adrenal glands from animals that those glands were indeed essential to life. It was Addison, however, who had been the first to show that a diseased condition could result from a defective ductless gland, and he can therefore be regarded with justice as the founder of endocrinology.

F. M. SUTHERLAND.

REFERENCE

[1] Bishop, P. M. F., *Proc. roy. Soc. Med.*, 1955, **48**, 1032.

The Science Museum Library has recently been presented with a collection of Japanese scientific and technical books and dictionaries on behalf of the Prime Minister of Japan, Mr. Nobusuke Kishi, and it now possesses a very complete collection of such recent books in English or with English summaries, in addition to current Japanese periodicals.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Development of Live Polio Vaccine

SIR,—Many will be interested in Dr. Hilary Koprowski's account of the historical aspects of this subject (July 9, p. 85), and, as he pointed out, some might produce a different version. I myself was sitting beside a well-known virologist in Copenhagen in 1951, when Dr. Enders described the successful growth of poliomyelitis virus in tissue cultures. After this important contribution my neighbour turned to me and said, "There is your answer for prevention—it will now be possible to prepare attenuated strains." Most students of poliomyelitis, therefore, expected the developments which Dr. Koprowski initiated in 1951, and the real mystery is to find out why these developments were pushed aside in 1954 in favour of the use of inactivated virus.

This decision was taken by the great National Foundation for Infantile Paralysis, and it seemed at the time to depend on factors which were more psychological than scientific. Attenuated strains were already available, and if at that time a hundred experts had been told a trial *must* now be held, should it be done by one method or the other, then most would certainly have favoured live oral attenuated virus as the method of choice, and one which carried less theoretical risks than the newly suggested use of inactivated virus injections. The reason for the surprising and I think unfortunate decision seemed to lie in the personality of the experts involved. Virologists represent a group of scientists who have a close international understanding with each other, and for whom all must have a great admiration. After Dr. Enders's great discovery, however, they seemed to be forced into positions they were unable to cope with. Tremendous political and national decisions had now come to depend on their advice. Every line of action involved some risk, yet action had to be taken, and the more famous the virologist the less was he prepared to make such decisions. The National Foundation, however, demanded action, and in due course found some who would act. What has happened in this country is of less interest, for we have rather uncritically followed the lead given by the National Foundation.—I am, etc.,

Oxford. W. RITCHIE RUSSELL.

A Doctor's Duty

SIR,—Under the above heading Dr. Brian Lodge (July 9, p. 145) regrets that the Bishop of Exeter should have suggested that "extraordinary means" involving great expense, etc., should not be used to prolong the life of old people. Reading the full text of the bishop's address (July 9, p. 128) it seems clear that the bishop has, in fact, only given his sanction to what has always been the practice of many conscientious doctors. It is only when we are asked to define an old person or an expensive drug that difficulty arises, and to enunciate a rule.

Medicine is an art which notoriously cannot be practised according to rule. It calls for the exercise of the enlightened judgment of the practitioner. I think that we should agree that to perform an oesophagectomy on an unexceptional man of 80 showed an error of judgment; so would the failure to remove the breast of an

otherwise healthy woman suffering from early carcinoma. But no rule can be made: the practitioner must advise what seems to him to be right after considering the circumstances of each particular case.

It is helpful to read in the same issue of the *Journal* (p. 140) the Winchester Address by Sir John Wolfenden on "Crime and Sin": the subject is very closely related to that of the Bishop of Exeter. The bishop quoted Clough's well-known couplet: "Thou shalt not kill but needst not strive officiously to keep alive." Unfortunately that couplet was intended by its author to have a somewhat cynical connotation. There is another quotation which I have heard but cannot trace which is quite innocent of cynicism. It is: "There is no moral obligation to prolong the act of dying."—I am, etc.,

Aldborough, Norfolk. ANGWIN EDDY.

SIR,—To judge from his sermon delivered to the B.M.A. at Torquay (July 9, p. 128), it is clear that the Bishop of Exeter is unenlightened in matters pertaining to old people. I am less concerned, however, with this aspect than the hurt and distress he has caused to many of my patients. He has injured their morale and made them feel insecure. His statement that "there does not seem to be any moral obligation to employ extraordinary means" to keep the very old alive, is to countenance negative euthanasia.

The care of the aged, irrespective of their medical, mental, or social disability, is a measure of the dignity and culture of a country. It is the privilege and responsibility of all of us to provide such care.—I am, etc.,

Geriatric Unit,
Langthorne Hospital,
London, E.11. J. DELARGY.

SIR,—I was surprised that Dr. Brian Lodge in his letter (July 9, p. 145) on the question of treatment required for old people does not mention anywhere the need for finding out what the patient himself wants. If he merely wants to be left alone to die as comfortably as possible we have no right whatever to strive officiously to keep him alive. If, however, he enjoys life and wants to continue it, no expense or trouble should be spared to help him. As a profession we are far too prone to neglect to ask ourselves the question, "What does this patient want?"—I am, etc.,

Colchester. M. E. LAMPARD.

SIR,—I was most pleased to read the article by the Right Rev. R. C. Mortimer, Bishop of Exeter (July 9, p. 128), and his concise exposition of Christian ethics in medicine. However, I feel that I must clarify the position of the Catholic obstetrician in cases of hydrocephaly where section is not practicable and vaginal delivery impossible.

A vertex presentation is tapped by a long serum-needle, *per vaginam*, into the anterior fontanelle. A breech presentation is allowed to proceed till the body is delivered and then the occiput drained by a similar technique, inserting the needle either into the skull just above the mastoid process or into the cisterna magna. When sufficient fluid has been removed to permit vaginal delivery, labour proceeds in a normal manner. There is doubtless grave risk to the foetus and it will probably die, so it is advisable to perform interuterine baptism prior to the operation. The child is born and it is *not* killed by the obstetrician. This is a simple operation to perform, more ethical than a destructive operation, and one which I have had occasion to perform. I also know of non-Catholic obstetricians who prefer this perilous but life-saving operation to the more negative approach of the school which carries the perforator to the base of the brain.—I am, etc.,

Bury, Lancs. TERENCE BIRKETT.

Streptomycin in Children

SIR,—At High Wood Hospital for Children, during the years 1950–9, streptomycin was used in combination with one of the other antituberculous drugs in a high proportion of tuberculous children requiring chemotherapy. Their ages ranged from under 1 year to 15 years and the daily dosage of streptomycin varied accordingly from 0.25 g. to 1 g. The duration of treatment was seldom less than three months and frequently much longer. Many children received an enormous amount of streptomycin by present-day standards without ill effect—as much as 481 g. in one girl. Again, for a group of 24 children discussed below, whose mean age was 12.3 years, the mean total dosage was 116 g., and, however "selected" this group may be from the statistical point of view, these figures undoubtedly give a rough idea of the order of dosage for the whole series.

Because Hinshaw and Feldman[1] had shown that, although streptomycin (in contrast to dihydrostreptomycin) affected mainly vestibular function, long-continued use could cause cochlear damage with consequent deafness, it was decided by one of (F. J. B.) that it would be a wise precaution to carry out periodic audiograms on all children receiving streptomycin. Between 1955 and 1959 inclusive more than 400 patients under the age of 16 years who were being given a course of streptomycin underwent audiometric tests. Practically all were tested at the beginning and at the end of the course of treatment in addition to routine check during the actual course of injections. The total number of audiograms was 1,350. In only 24 children was any abnormality found. However, in 8 of these 24 there was some gross cause of deafness such as chronic mastoiditis or otorrhoea; or deafness was known to have preceded the administration of streptomycin. One child was a mongol. In a further 10 the loss was trivial and within the limits of experimental error, or alternatively was slight, present in the first audiogram before, or immediately after, beginning streptomycin treatment, and remained unchanged throughout the course. In yet another two children with significant loss on respectively the lower and (unilaterally) higher tones, considerable amounts of streptomycin had already been given elsewhere before admission to High Wood and consequently before the first audiogram, and it was not possible in them to assess the part, if any, played by streptomycin. In none of the 21 patients so far mentioned, moreover, was there any evidence of vestibular disturbance.

Of the three remaining children, one, a girl of 15 years, developed vertigo and doubtful nystagmus after 17 g. streptomycin, and was found to have negligible loss in the high-frequency range. A girl aged 9 with a normal audiogram before treatment was found to have a loss of 40 decibels at 8,000 cycles per second after 115 g. of streptomycin without evidence of vestibular disturbance. Lastly, a boy of 15 suffering from miliary tuberculosis was known to have been deaf in his right ear for three years, and before treatment had a grossly defective right but a normal left audiogram. After 74 g. of streptomycin he developed tinnitus, and after a further 13 g. nystagmus and slight Rombergism. His left audiogram now showed a loss of 40 decibels at 8,000 cycles per second.

Although every child on streptomycin was naturally watched for clinical evidence of vestibular disturbance, only the presence or absence of a positive Romberg test was recorded as a routine, and this is doubtless a crude test in comparison with, for example, caloric tests. Among these children on streptomycin a positive Romberg test was found in only four and a doubtful positive in seven. This certainly does not represent the total number of vestibular reactions, but nevertheless we have the strong clinical impression that that total was very small indeed.

These findings indicate that prolonged treatment with streptomycin (as opposed to dihydrostreptomycin) very rarely causes cochlear damage in children, and in our experience even slight vestibular damage is also rare. This is in striking contrast to the position in the middle-aged and elderly; Cawthorne and Ranger[2] reported 22 cases of ototoxicity developing in patients receiving 16 g. of streptomycin or less.—We are, etc.,

M. A. BAQAI.
G. LORRIMAN.
F. J. BENTLEY.

High Wood Unit,
Black Notley Hospital,
Essex.

REFERENCES

[1] Hinshaw, H. C., and Feldman, W. H., *Proc. Mayo Clin.*, 1945, **20**, 313.
[2] Cawthorne, T., and Ranger, D., *Brit. med. J.*, 1957, **1**, 1444.

Diabetes Insipidus after Tuberculous Meningitis

SIR,—If there is a competition in describing cases of diabetes insipidus following tuberculous meningitis, may I hastily claim third place in Britain, by a short head? I described such a patient (white) in the course of a recent article on tuberculous meningitis,[1] which Dr. J. P. Wall (July 2, p. 68) has not noticed.—I am, etc.,

ARNOLD PINES.

Department of Tuberculosis
and Diseases of the Respiratory System,
University of Edinburgh.

REFERENCE

[1] Pines, A., *Tubercle (Lond.)*, 1960, **41**, 119.

Appendicitis in Pregnancy

SIR,—I was interested in Dr. W. P. Black's article (June 25, p. 1938). The fatality described raises the old question of the management of the late case. Is it not likely that conservative treatment at this stage of the appendicitis (sixth day) would have given a better chance of survival than appendicectomy, with the inevitable further dissemination of the inflammatory process?—I am, etc.,

J. M. MOORE.

Victoria Infirmary,
Glasgow.

The Eye of the Premature Baby

SIR,—In your recent annotation (July 2, p. 45) you question the belief that hyaloid vessels persist in the eyes of premature babies. Without being able to give detailed figures, I can throw a little light on the problem. In a survey already published[1 2] my colleagues and I had access to 729 successive admissions to two large premature units. All babies were examined within the first week of life, although none on the first day.

It was very rarely that we failed to see persistent hyaloid remnants in the eyes of infants of birth weight of 3 lb. (1.36 kg.) and under; over this birth weight they were very uncommon. These remnants varied from one single wisp of gauzy filament to a branching frond of black strands moving like seaweed in the vitreous. We *never* observed functioning hyaloid vessels in any of our cases: all were remnants. In all cases the remnants disappeared before discharge from the units. The behaviour of the hyaloid remnants was not affected in any way by changes in the policy of oxygen administration, which varied during the period under review from an extremely generous allowance in 1951 to a basic minimum in 1953 to 1954.—I am, etc.,

R. M. FORRESTER.

Royal Albert Edward Infirmary,
Wigan.

REFERENCES

[1] Forrester, R. M., Jefferson, E., and Naunton, W. J., *Lancet*, 1954, **2**, 258.
[2] —— M.D. Thesis, 1955. Cambridge.

Sleep and Rhythmic Stimulation

SIR,—May I reply to the comments by Dr. John Evans (June 11, p. 1808) concerning my paper (May 14, p. 1450) on falling asleep during intense rhythmic stimulation?

It is an all-too-common misconception that there is a relationship between human hypnosis—that is, the state produced by a hypnotist—and the state of sleep. There *may* be such a relation, but it has yet to be discovered. The state of so-called "animal hypnosis" has been shown to have physiological concomitants characteristic of light sleep, such as bradycardia and also the E.E.G. changes.[1–4] It can be produced by rhythmic stimulation, overwhelming stimulation, forcible bodily restraint, or any combination of these.[5] In extreme cases death may rapidly follow.[6] It is very different from human hypnosis, and I would agree with writers such as Weitzenhoffer[7] who conclude that there is no evidence that the two are identifiable. On the contrary, there have been numerous investigations which have failed to find any change in recordable physiological function characteristic of human hypnosis, and have shown that human hypnosis appears to be a state of wakefulness and not a state of sleep.

Confusion is bound to follow from the usage of the term "hypnosis," which, by its derivation, implies sleep. Sleep suggestions are commonly made during the induction of a human hypnotic trance. They are unnecessary[8] for the production of a trance state in which all the usual phenomena of hypnotism can be elicited. It is common experience that suggestions of drowsiness together with repetitive stimulation (which itself tends to provoke relaxation) facilitate the induction of human hypnosis, but I suggest that they do so because, in relaxation and drowsiness, there is a decrease in the tendency for the individual to react in a critical manner to environmental stimuli, so increasing his tendency to respond to the hypnotist's suggestions. Numerous authors, including Barker and Burgwin[9] in the well-known paper to which Dr. Evans refers, have shown that, electroencephalographically, human hypnosis is not sleep, but that, just as other hypnotic suggestions may be successful—for example, of gaiety—so may suggestions of sleep combined with immobility and restricted stimulation be followed by true sleep, in which, however, hypnotic rapport is lost. I would agree that the subjects of my experiments passed into a state of *animal* hypnosis. There are no grounds on which to base a view that they passed into a state comparable to that produced by the conventional human hypnotist.

Finally, I personally do not like Pavlov's term "transmarginal inhibition," preferring the concepts of Western neurophysiology. Pavlov[10] correctly identified animal hypnosis with sleep, but was wrong in similarly identifying human hypnosis, as has subsequently been shown by a variety of physiological studies (translation difficulties may be partly at fault). It should, in any case, have been apparent, since in a state of cortical internal inhibition, to use Pavlov's terms, conditioned responses are diminished, whereas in human hypnosis

the subject responds as well as or better than normally to such signals as the hypnotist wishes.—I am, etc.,

Department of Psychological Medicine, University of Edinburgh. IAN OSWALD.

REFERENCES

1 Gerebtzoff, M. A., *Arch. int. Physiol.*, 1941, **51**, 365.
2 Schwarz, B. E., and Bickford, R. G., *J. nerv. ment. Dis.*, 1956, **124**, 433.
3 Svorad, D., *Arch. Neurol. Psychiat. (Chicago)*, 1957, **77**, 533.
4 Silva, E. E., Estable, C., and Segundo, J. P., *Arch. ital. Biol.*, 1959, **97**, 167.
5 Gilman, T. T., and Marcuse, F. L., *Psychol. Bull.*, 1949, **46**, 151.
6 Richter, C. P., *Psychosom. Med.*, 1957, **19**, 191.
7 Weitzenhoffer, A. M., *Hypnotism*, 1953. Chapman and Hall, Ltd., London.
8 Wells, W. R., *J. abnorm. soc. Psychol.*, 1923, **18**, 389.
9 Barker, W., and Burgwin, S., *Arch. Neurol. Psychiat. (Chicago)*, 1949, **62**, 412.
10 Pavlov, I. P., *Selected Works*, 1955. Foreign Languages Publishing House, Moscow.

Prothrombin Time Abroad

SIR,—I write as a full-time salaried consultant clinical pathologist who undertakes the management of the anticoagulant therapy of patients who are on maintenance doses of, e.g., phenindione, in collaboration with these patients' general practitioners. From time to time a patient will travel on the Continent of Europe, and so will be out of reach for some weeks or even months. In such cases it would be very desirable to be able to instruct the patient to call at a specified date at a specified laboratory to have his prothrombin time checked. Such a patient should carry instructions from England that his prothrombin time (Quick) should be kept between certain limits (in my case between 2 and 2½ times the normal control time) and that his dosage has been so many milligrammes of such and such a drug.

I know of laboratories in Nice and in Zurich where such tests can be done and where—this is important—the reports detail the actual observed prothrombin times of patient and normal control; I am anxious to expand this information to the point where we have a list of such laboratories in the major cities of the most-visited parts of Europe. I would stress the importance of the reports containing the observed times in seconds, as it is quite simple to instruct a patient as to the desirable range on this basis, and such information will enable the patient to check that changes in his dosage recommended by local doctors are of the kind he would expect. This is essential because there are at least two other ways of expressing the results of the Quick test; not to mention newer fashions using techniques such as Owren's prothrombin and proconvertin and its later version the "thrombotest." All these give results which cannot be related to the instruction that the Quick prothrombin time be kept between 2 and 2½ times the normal control time—at least not by any simple procedure. I would wish to instruct my patients to pay no attention to so-called prothrombin activity, or prothrombin index, or percentage prothrombin by any other technique; but to observe that the normal control time should lie as near to 12 seconds as can be, and should not be longer than 18 seconds at the most (a safeguard against the use of suboptimal reagents—a phenomenon which I have encountered in patients referred from other hospitals in England. If any of your readers can help in the compilation of such a list of laboratories and/or doctors I should be grateful for their assistance in this matter.—I am, etc.,

New End Hospital (Archway Group), New End, Hampstead, London, N.W.3. A. F. MOHUN.

Visual Acuity Surveys

SIR,—The work of Professor Arnold Sorsby and his collaborators on refraction and its abnormalities is deservedly known and admired all over the world. Their latest contribution (May 7, p. 1394) is of great interest to those of us who have ventured into this difficult field where little has so far been done. I would only point out that mention should have been made of the contribution of Pendse[1] and that our own observations on the children of two East African Bantu tribes published recently[2] may also interest Professor Sorsby.

A further study we have undertaken of the refraction of Indian schoolchildren in East Africa, in which many of Pendse's findings are confirmed, is in the course of preparation for publication. May I also reiterate Pendse's plea for standardization of the method of expressing refraction data of this kind? Perhaps this might most appropriately be taken up at the XIX International Congress of Ophthalmology to be held in New Delhi in 1962.—I am, etc.,

D. S. MCLAREN.

East African Institute for Medical Research, Mwanza, Tanganyika.

REFERENCES

1 Pendse, G. S., *Indian med. Res. Mem.*, 1954, No. 38. Central Research Institute, India.
2 McLaren, D. S., *J. trop. Med. Hyg.*, 1960, **63**, 101.

Recurrent Intussusception

SIR,—Recurrent intussusception is rare. Bailey and Love[1] say it occurs in 2% of cases of idiopathic intussusception; Gross[2] mentions the same figure and says that the largest number of recurrences ever reported in one individual was in a child who required four operations. In the case to be described the intussusception occurred three times and three different varieties of it were seen.

A 10-year-old Yoruba boy was admitted to the medical ward of Adeoyo Hospital on December 12, 1959, with a month-old history of colicky abdominal pain and occasional vomiting. There was a slight loss of weight and he was somewhat constipated. No blood was passed per rectum. On examination his general condition was good. The abdomen was not distended. A non-tender, ill-defined mass was felt across the abdomen above the navel. Bowel sounds were prominent. Rectal examination was negative. A blood count, urine and stool examination, and radiographs of the abdomen were not helpful. A dose of piperazine was given, the mass moved to the left lumbar region of the abdomen, but no roundworms were passed.

Two days later a laparotomy was done. The mass was then felt in the epigastrium and an upper midline cut was made. An iliocaecal intussusception was easily reduced, and as the patient's condition was good his appendix was removed and the stump buried in the usual way. Three days after this, he developed colicky abdominal pain with visible peristalsis and a mass in the right inguinal fossa. The wound was opened up and an ileo-ileal intussusception reduced with ease. He made good progress and was discharged on January 4, 1960. He reported again three weeks after this with a four-day history of abdominal pain, constipation, and occasional vomiting. The abdomen was distended. There was a ladder pattern of small bowel and a sausage-shaped swelling was palpable in the left inguinal fossa. The scar of the previous operations was excised and a caecocolic intussusception found and reduced but not as easily as on the first two occasions. On February 5 he had his fourth and, we hope, last episode. A lower midline incision was used and a caecocolic intussusception was reduced with considerable difficulty. The lower end of the caecum was stitched to the lateral abdominal wall with the

aim of preventing this type of intussusception. The patient's condition was rather poor after this operation, but he soon improved and was discharged well three weeks later.

In West Africa, although infantile intussusception is occasionally seen, its main incidence is in children aged 5–10, and the common variety is the caecocolic.[3] Caecocolic intussusception is the commonest cause of acute or subacute intestinal obstruction in West African children. In this country (Nigeria) when a lump is ill-defined or not palpable it is difficult to distinguish intussusception from roundworm obstruction, and it is said that 25% of cases opened up for intussusception are found to have roundworm masses.[3] The patient described had a persistent ascending mesocolon, which is much commoner here than in Europe. This permitted the development of his two caecocolic intussusceptions which may well have had their origin in the buried stump of the appendix. The cause of the ileocolic and ileo-ileal varieties was not found.—I am, etc.,

Adeoyo Hospital, Ibadan, Nigeria. R. O. PARNIS.

REFERENCES

1 Bailey, H., and Love, McN. (1959). *A Short Practice of Surgery*, 1959, 11th ed. H. K. Lewis, London.
2 Gross, R. E., *The Surgery of Infancy and Childhood*, 1953. W. B. Saunders, Philadelphia and London.
3 Trowell, H. C., and Jelliffe, D. B., *Diseases of Children in Subtropics and Tropics*, 1958. Edward Arnold, London.

Pulseless Disease

SIR,—From time to time syndromes characterized by absence of pulsation of arteries arising from the arch of the aorta have been reported. In view of the fact that more than one pathological lesion may be responsible for such syndromes they have been described under various names. Any case of slow obliteration of arterial pulsation can be called a pulseless syndrome, and any case with absence of pulsation in all the arteries arising from the aortic arch can be called aortic-arch syndrome. The effect of loss of blood supply distal to the occlusion in such cases is likely to be the same irrespective of the pathological lesion. Of the pulseless syndromes the one which goes with Takayasu's name occurs in young women, has a pathological picture of non-specific arteritis, and has been often referred to as the pulseless disease. That does not necessarily mean that absence of pulsation in the arteries in young women must always be due to such non-specific arteritis (*vide infra*), or that Takayasu's pulseless disease has any specific clinical feature of its own. The following summary of a case under my observation may be illustrative.[1]

A woman of 35, mother of five normally born healthy children, was first seen for some eye complaint which was later diagnosed as allergic scleritis. She had also a cough which was successfully treated. During physical examination it was accidentally discovered that the pulsation in the arteries of her upper limb was totally absent. But the carotid pulsation was present and was associated with a systolic thrill and murmur. There was also a strong suprasternal pulsation. There was no abnormal finding in the heart. Blood-pressure could not be recorded in the upper limbs. The popliteal artery pressure was 174/90 mm. Hg. A vascular bruit was present in the intercostal spaces indicating increased blood flow. The fundus did not show any abnormality.

On inquiry the patient said that since her childhood there had been some abnormality in her pulse, as her doctor always used to comment, and her pulse was always palpated in the neck. The E.C.G. was normal and phonocardiogram confirmed the circulatory findings. Unfortunately aortography, arteriography, or arterial biopsy could not be done.

The lesion must be at the origin or along the course of the arteries of the upper limbs and, without much doubt, congenital in nature. Whatever be the exact anomaly, we can, for descriptive purposes, call it an aortic-arch syndrome and not Takayasu's disease or young female arteritis, although the patient happens to be a young woman.—I am, etc.,

Bankura Sammilani Medical College, West Bengal. S. N. SEN GUPTA.

REFERENCE

1 Sen Gupta, S. N., *Bull. Calcutta Sch. trop. Med.*, 1958, **6**, 88.

Backache and Gardeners

SIR,—I think that most practitioners must be aware of the immense problem that backache now presents to the orthopaedic departments of most hospitals. Quite a large number of the sufferers are also gardeners, and find it very difficult to pursue their hobby on account of this trouble. Because of this, I designed an apparatus which would help those with backache to accomplish many of the jobs in the garden which call for stooping or kneeling, without having to bend their backs, or endure the damp discomfort of kneeling.

Essentially the apparatus is a light metal box, curved at the front edge, so that it has a rolling or rocking action, and by leaning forwards the reach of the user, still maintaining a straight back, is considerably increased. It has proved successful, and can be used for planting, pruning, weeding, and picking fruit, as well as for many other jobs that require a low mobile stool. The box acts as a container for the reception of the material which is to be planted, or the rubbish collected.

It is made by Chase Protected Cultivation Ltd., of Shepperton, Middlesex, and marketed by them under the name of Chase Chug.

—I am, etc.,

Kettering General Hospital, Northants. FRANK RADCLIFFE.

Hypothermic Coma in Myxoedema

SIR,—The article entitled "Hypothermic Coma in Myxoedema," by Drs. J. H. Angel and L. Sash (June 18, p. 1855), stimulates discussion respecting the management of myxoedematous coma. A study of the relevant literature shows that recovery from myxoedematous coma has been exceptional, and that the treatment adopted has usually consisted in (1) strenuous attempts to combat associated hypothermia by means of electric blankets, heat cradles, etc.; and (2) the rapid introduction of large doses of thyroid hormone into the patient's body. In a number of cases these measures have been supplemented by the use of corticosteroids in an effort to combat any concomitant adrenal insufficiency that may be present.

The melancholy fate of the majority of patients admitted to hospital suffering from impending or actual myxoedematous coma prompts one to appraise critically the

aforesaid "logical" regimen of treatment. The precipitate application of heat to subjects in a state of hypothermic coma caused by myxoedema must have the effect of accelerating the physiological activities of the tissues, thereby increasing the oxygen requirements of the latter. Moreover, the *rapid* introduction of large amounts of thyroid hormone into the system of these comatose subjects must likewise result in a marked acceleration of cellular metabolism and oxygen utilization. This point is underlined by the fact that the survival time of animals placed in a closed vessel is decreased after the administration of thyroxine or triiodothyronine.[1] It is likely that in many instances of myxoedematous coma the patient's cardiovascular system (impaired by the effects of long-standing hyperthyroidism) is unable to cope with a sudden augmentation of the amount of oxygen needed by the tissues, and that this state of affairs can lead to disaster. In regard to the problems involved in the treatment of patients in myxoedematous coma, it is noteworthy that Macdonald[2] has concluded that "rewarming is illogical and probably dangerous," and Nieman[3] that intravenous triiodothyronine has brought no improvement and may indeed be dangerous in producing a too rapid acceleration of metabolism."

The writer suspects that an exaggerated sense of urgency is out of place in the management of these cases, and that one should instead "make haste slowly" in the matters of rewarming the patient and prescribing thyroid hormone. In addition to the routine employment of antibiotic agents, the treatment of these patients should perhaps include the exhibition of a small dose of phenobarbitone as subjects with severe myxoedema are prone to epileptiform fits,[4 5] the advent of which may herald a sharp deterioration in their condition (see case 2 of Le Marquand *et al.*,[6] and cases 1 of Malden[7] and Macdonald,[2] respectively). That myxoedematous patients in a stuporose or comatose state (and seemingly moribund) *can* respond to relatively simple and unhurried methods of treatment is evident from reports that have appeared in the medical literature.[8 9]—I am, etc.,

Menston Hospital,
Ilkley, Yorks.

J. TODD.

REFERENCES

1 Duncan, G. G., *Diseases of Metabolism*, 1959. W. B. Saunders, London.
2 Macdonald, D. W., *Brit. med. J.*, 1958, **2**, 1144.
3 Nieman, E. A., ibid., 1959, **1**, 1204.
4 *Trans. clin. Soc. Lond.*, 1888, **21** (supplement).
5 Bleuler, E., *Textbook of Psychiatry*, 1924. Macmillan, New York.
6 Le Marquand, H. S., Hausmann, W., and Hemsted, E. H., *Brit. med. J.*, 1953, **1**, 704.
7 Malden, M., ibid., 1955, **2**, 764.
8 Martin, L., and Whittle, C. H., ibid., 1953, **1**, 1108.
9 Todd, J., and de Zilwa, H., *Med. Press*, 1954, **232**, 298.

SIR,—I was much interested in the article on "Hypothermic Coma in Myxoedema" by Drs. J. H. Angel and L. Sash (June 18, p. 1855), and am prompted to report a further case.

A 72-year-old woman was brought to the casualty department of Northampton General Hospital at 5.30 p.m. on November 27, 1959. She was said to live alone. As her neighbours had not seen her for a few days, they informed the police, who entered the house and found the patient unconscious. No further history was available. On examination, she was unconscious but groaning and grinding her teeth. She was obese, and extremely cold. The body temperature could not be recorded on an ordinary clinical thermometer. A water-bath thermometer inserted into the rectum gave a reading of 70° F. (21.1° C.). The patient was malodorous and teeming with body lice, which had caused widespread ulceration of the skin. The general appearance of the face and the texture of skin and hair suggested myxoedema. The pulse was regular, rate 40 per minute, and the blood-pressure was 100/70 mm. of Hg. The heart was a little enlarged. The mitral first sound was accentuated, and there was a soft, short apical systolic murmur. A little pitting oedema was present over legs and sacrum. No significant abnormality was detected in lungs, abdomen, or nervous system. A clinical diagnosis of myxoedema coma was made. The electrocardiogram showed sinus bradycardia, low voltage complexes, and flat T waves.

The patient was warmed with a heat cradle while thyroid, gr. 1 (65 mg.), was introduced through a stomach tube. At 10.20 p.m., five hours after admission, the rectal temperature had risen to 82° F. (27.8° C.), and the patient had regained consciousness. She tried to speak, but her voice was very thick and low and her speech unintelligible. At this point heating was discontinued. An hour later, at 11.30 p.m., the general condition improved, and the speech was now easily understood. The voice was characteristic of myxoedema. The temperature was now 84° F. (28.9° C.), and the blood-pressure 100/70 mm. Hg. The heart, however, now showed auricular fibrillation with a ventricular rate of 108/min. There was moderate pulmonary congestion. The heart failure became worse during the night in spite of treatment with intravenous and oral digoxin, mersalyl, and intravenous aminophylline. Steroids were not used. At 6.15 a.m. on November 28 she once more became unconscious, in spite of the fact that the temperature had risen to 88° F. (31.1° C.). At 8.15 a.m., nearly fifteen hours after admission, she died.

At necropsy, the skin was covered with the scabs of pediculosis-corporis infection and there were some large areas of superficial ulceration. The thyroid gland weighed 19 g., was uniformly decreased in size, light brown in colour, and slightly fibrotic and atrophic on section. Histological examination showed that the acini were small or very small, with considerable reduction of colloid except in one or two areas. There was some increase in parenchymal fibrosis, and a very minor degree of lymphoid infiltration was present, without lymphoid-follicle formation. The mitral valve was narrowed, with evidence both of old rheumatic valvular disease and of active rheumatic endocarditis. The aorta and the coronary arteries were atheromatous. There was an ulcer, 2.5 cm. in diameter, in the lower third of the oesophagus. Death was due to myocardial failure and myxoedema hypothermia.

This patient is of interest, first because on admission the body temperature was lower than in any other published record of this condition, and second because re-warming temporarily restored consciousness, which was not the experience of Drs. Angel and Sash. In the case reported here, time was too short for the thyroid administered by stomach tube to have had any influence upon the course of the illness.—I am, etc.,

General Hospital,
Northampton.

B. K. SAMTANI.

Inoculation Technique

SIR,—Having seen the letters in the *Journal* concerning the need for an efficient one-way valve between needle and syringe, to be used in inoculation and vaccination techniques, may I be allowed to draw your

attention to a valve which may be suitable? It was originally designed to maintain a patent needle and no syringe-reflux during prolonged intravenous work. The valve is designed on the same principle as a bicycle valve and may be sterilized and re-used. It is being made by M.I.E., London, and is now in their catalogue: p. 170, Fig. 4013—Heller's Adaptor.—I am, etc.,

Wakefield. M. H. HELLER.

Laissez-faire Antenatal Care

SIR,—Replying to Mr. F. Langford's letter (July 9, p. 149) and emphasizing that I write as an individual who just happens to have been on the Norfolk Local Medical Committee for 12 years, I too read Dr. Hamish G. Nicol's letter (May 14, p. 1504), but without surprise: because (1) in the B.B.C. television programme "Your Life in Their Hands" a town G.P., presumably supposedly considered a fair sample, showed that he had no intention of doing any more for his "Period 1" fee than take the blood-pressure and test the water on two occasions. (2) We on the Norfolk L.M.C. have for many years pressed that, whether a bigger fee was allowed or no, the minimum standards for Periods 1 and 2 should be raised considerably, and, though obtaining it in this county by voluntary effort, have received no support from the Powers that Be.—I am, etc.,

Cromer, Norfolk. A. H. GREGSON.

Retained Cord

SIR,—I wondered if the following true account might be of interest to your readers.

A Mosuto woman aged 25 (para-4) arrived at the Queen Elizabeth II Hospital, Maseru, at 3 a.m. on April 24 with a newborn baby and its placenta, but with the end of the umbilical cord apparently still *in utero*, the other end (which had been attached to the baby) protruding from her vulva. She had been delivered normally of a live baby girl by her mother-in-law 15½ hours previously. After intermittent severe bleeding the placenta had been finally delivered 6½ hours later, but the cord had remained firmly *in utero*. The patient was then brought 21 miles by car over rough roads to Maseru.

On examination on admission the cord was found firmly attached, but there was no bleeding from it; the placenta appeared complete, but the membranes had torn off all round its circumference; the uterus was normal post-partum size. After 6 hours' observation there had been no delivery of the cord, so an examination under anaesthesia was carried out. The cord was found to go up into the uterus, which also contained the membranes unseparated. These, with the cord, were separated digitally, removed, and examined. A velamentous insertion of the cord was revealed. The cord had thus been held *in utero* by the separated membranes while the placenta had separated, torn off the membranes at its circumference, and delivered itself.

—I am, etc.,

Maseru, Basutoland. J. H. DALY BRISCOE.

Long Cord

SIR,—I was recently called to one of my confinements at the urgent request of the midwife because the cord was prolapsed. The patient was a primigravida, slightly toxaemic, aged 33 years. She lived about four miles from my house, and I think I only took about fifteen minutes to get there. When I arrived I found a good-sized loop of cord protruding from the vulva. The head was on the perineum, so I quickly applied forceps and delivered a dead female child, as I had expected I should. The cord measured 65 in. (165 cm.) from its insertion in the placenta to the umbilicus. I am most interested as to whether this approaches a record for an abnormal length of cord. Nowhere in my meagre library can I find any figures to assess my experience.

I may add that the mother has been married twelve years and this was a very much wanted pregnancy, she not having been able to conceive until this pregnancy.—I am, etc.,

King's Lynn, Norfolk. PETER F. R. LANKESTER.

High-pressure Salesmanship

SIR,—The letters from Dr. S. Bradshaw and Mr. F. R. Zadik (July 9, p. 151) show, I think, the present ridiculous state of affairs whereby we are literally bombarded with medical advertisements by post. Might I suggest an excellent remedy which costs little and is well worth the time? It consists of sending a postcard to the more persistent offenders asking for one's name to be removed from the mailing list. I have also asked most of the other firms to send only one advertisement to our house instead of sending one for me and one for my wife. It is amazing that prior to this only one drug firm showed the initiative to send one envelope addressed to both of us.

If anything is apt to put me off a particular firm it is a display of wastefulness. Either the right hand does not know what the left hand is doing, or, if it does, the expense matters little in any case. Personally I prefer reading about drugs in the journals, or discussing them with representatives at intervals of not less than six months.—I am, etc.,

Holmes Chapel, Cheshire H. T. N. SEARS.

SIR,—In view of the increasing number of representatives of medical firms who have been calling upon us, we have introduced the system of obtaining their signature in a special notebook, and then informing them that it is useless for them to visit us again for a period of less than six months, unless, of course, the firm has produced some important new product in the meantime. It might interest other practitioners to know of this arrangement, and also the fact that to date we now have a record of 50 different firms who send representatives to general practitioners.—I am, etc.,

Liverpool, 4. MONTAGUE SOLOMON.

SIR,—Dr. S. Bradshaw's letter (July 9, p. 151) suggests that, if any doctor has a worthwhile alternative to the welter of direct-mail material sent round to the medical profession, he should communicate at once with the nearest pharmaceutical house.

A short time ago, when this firm sent out a questionary as to the methods doctors preferred for obtaining information on ethical medical products, no less than 88% of the 1,110 doctors who replied stated their preference for articles and clinical reports published in the medical journals.

Some day I feel sure the leading pharmaceutical houses will reproduce in your advertisement pages accurate abstracts of clinical reports on their products for the benefit of those who may have missed reading

the originals. Apart from the fact that such a method of promotion is likely to be acceptable to the majority of the medical profession, it is also likely to assist them in either maintaining or building their standing as a reputable pharmaceutical concern *pari passu* with the most effective way of advertising their products.

While in no way disputing Dr. Bradshaw's facts regarding sample returns, these can scarcely be regarded as the sole criterion of the efficacy of this method of promoting ethical products, especially since so many doctors are allergic to it.—I am, etc.,

MAURICE KEATING,
Director, Harley Publishing Co. Ltd.

London, W.C.2.

Self-medication

SIR,—I recently came across a young man who presented with general malaise, profuse sweating, and a pyrexia of 101° F. (38.3° C.). My suspicions were aroused by the fact that he had a pulse rate of 72. The cardiovascular system revealed a hypertension of 180/110 and an aortic systolic bruit. On further questioning, it appeared that after having felt ill for about an hour a friend persuaded him to take four "preludin" (phenmetrazine) tablets, which he claimed had no effect on him.

The following morning the B.P. was down to 150/100 and the heart sounds were normal. I began salicylate treatment and 24 hours later his symptoms had improved—temperature 99° F. (37.2° C.), pulse 84, and B.P. now at 125/70. On the third day he was completely recovered from his illness. In conclusion I presume that this shows the sympathomimetic effect of phenmetrazine complicating the course of a simple illness. Needless to say, the patient was warned against the habit of accepting tablets at random.—I am, etc.,

D. J. ELLAM.

Littleover, Derby.

Adoption

SIR,—Since Lady Lewis in her article on adoption (April 16, p. 1197) has adequately covered the questions raised by Dr. Joan Wagstaff (May 7, p. 1429) she really needs no defending. I would like to comment, however, lest other readers also have overlooked the same points. Sociologists have long been aware that parents of illegitimate children, just as parents of legitimate infants, tend to come from the same socio-economic class. The realistic authors such as De Maupassant and Zola have usually portrayed seductions in this fashion.

Examination of the data of Skodak and Skeels,[1] from whose work the comment about an I.Q. difference of 20 points was taken, shows that the education of the true fathers is very similar to that of the true mothers, just as is the case with the foster parents, who have similar educational backgrounds but at a much higher level. Their findings are shown in the following table:

Education of Parents of Adopted Children

	True Fathers	True Mothers	Foster Fathers	Foster Mothers
Less than 8th grade ..	15·3	13·1	3·0	6·0
8th grade	22·0	25·0	23·0	9·0
9th, 10th, 11th grade ..	21·8	27·2	14·0	16·0
High-school graduate ..	25·4	26·0	16·0	18·0
1–3 years college	10·1	8·7	23·0	35·0
College graduate	3·4	—	10·0	14·0
Postgraduate	—	—	11·0	2·0
	98·0	100·0	100·0	100·0

Almost 40% of the natural mothers and fathers had an 8th grade education or less while only 13.5 and 8.7%, respectively, went beyond high school. In contrast, 44% of the foster fathers and 51% of the foster mothers had some college education. The true parents both come primarily from the two lowest occupational groups. Lady Lewis's own figures are quite similar, indicating a close correspondence between the natural mother and putative father and a much higher occupational level for the adoptive father. Since there is a close association between education, occupation, and I.Q. score, the data would suggest that the intelligence of the fathers is not a major factor in the difference that is found in adopted children. Furthermore, others have shown that enriching the environment by such things as nursery-school attendance will raise the I.Q.s of children who are living in their own homes.[2]

It would appear difficult for some professionals to question the belief that they are innately superior and accept the fact that they may have attained their status because their environments have been more favourable. Action to improve the conditions of life cannot degrade those who are doing well, but can only raise the general level of the entire population.—I am, etc.,

HILDA KNOBLOCH.

Clinic of Child Development,
Children's Hospital,
Columbus, Ohio.

REFERENCES

1 Skodak, M., and Skeels, H. M., *J. genet. Psychol.*, 1949, **75**, 85.
2 *39th Yearbook of the National Society for the Study of Education*, 1940. Nature and Nurture. Part I. Their Influence upon Intelligence. Public School Publishing Co., Bloomington, Illinois.

First-Aid in Aircraft

SIR,—Having read Dr. F. Reynolds's letter (June 4, p. 1739) and the able replies of Dr. K. G. Bergin and Dr. A. Buchanan Barbour (June 25, p. 1958), may I be permitted to state the position as it applies to Aer Lingus—Irish International Airlines?

Each aircraft of Aer Lingus—Irish International Airlines—carries: (*a*) Three large emergency first-aid kits which contain an assortment of medical items, including "tubonic" ampoules of "omnopon." These large emergency kits are sealed and can only be opened on the authority of the captain of the aircraft. If the captain authorizes the opening of any of these emergency first-aid kits, he must make an entry in the aircraft technical log and re-seal the kit after use. (*b*) One small medical first-aid kit, containing a small supply of simple medicaments and dressings (including analgesics). This first-aid kit is under the care of the air stewardess and is refurbished after each flight.—I am, etc.,

SEAN O'QUIGLEY,
Medical Adviser,
Aer Lingus—Irish International Airlines.

Dublin Airport.

SIR,—Having read with some astonishment the remarks of Dr. F. Reynolds (June 4, p. 1739) criticizing the provision of first-aid in aircraft, I was pleased to see the replies from the medical services of B.O.A.C. and B.E.A. (June 25, p. 1958). I would like, however, to add that this question has been thoroughly studied in other airlines than the British ones.

Ideally, perhaps, all hostesses ought to be trained nurses because of their responsibilities in looking after so many passengers of varied ages and states of health. In practice, however, this is impracticable, as not enough trained nurses apply for hostess training.[1]

Most larger airlines, however, carry well-equipped first-aid kits, the contents of which are under constant review by the respective company medical services. Hostesses and stewards

are trained in the use of these kits by the company doctors. As well as the usual bandages, etc., and various pharmaceutical preparations shown by experience to be most needed by passengers and crews, these kits contain adequate oral analgesics of several types and, in some cases, "tubonic" injection kits (or similar) containing "pantopon." In this case the cabin crews are trained in the injection procedure by using dummy kits containing physiological saline. Any use of these injection kits must be authorized by the captain of the aircraft. Apart from these kits, to be used in case of necessity during flight, jets carry a separate emergency kit which is sealed and belongs to the aircraft, and further supplementary kits are carried as part of the ditching-kit in aircraft flying over the sea.

I feel, therefore, that the general criticism implicit in your correspondent's letter is not actually justified, and hope that these remarks—together with those from B.O.A.C. and B.E.A.—will convince him that his unfortunate experience does not constitute a true picture of the general situation.—I am, etc.,

Zürich Airport, Switzerland.

R. GRAEME CAMERON,
Medical Officer, "Swissair"
(Swiss Air Transport Company Ltd.)

REFERENCE

[1] McFarland, Ross A., *Human Factors in Air Transportation*, 1953. McGraw-Hill, New York.

Gentlemen Boxers' Brains

SIR,—Can Drs. F. B. Byrom and P. M. Daniel (July 9, p. 153) provide material evidence that transient unconsciousness as suffered by boxers causes permanent damage to the brain? We have examined hundreds of amateur boxers who have sustained concussion, and all neurological, psychometric, and encephalographic studies have been negative.—We are, etc.,

London, S.W.1.

J. L. BLONSTEIN,
J. SHARP GRANT,
Honorary Medical Officers,
Amateur Boxing Association.

Diploma in Dermatology

SIR,—Dr. John C. Belisario, writing from Australia (June 18, p. 1892), says that he knows of no other fellowship qualification in the British Commonwealth, with the exception of the F.R.C.P. Edinburgh, in which a reasonable knowledge of dermatology is required. There is one: the F.R.C.P. Canada.

The way to official recognition as a dermatologist in most parts of Canada is to acquire the certification in dermatology of the Royal College of Physicians of Canada. Subsequently one may elect to try for the even higher qualification in one's specialty, and become F.R.C.P. Canada.—I am, etc.,

Department of Pathology,
University of Michigan, U.S.A. BERNARD NAYLOR.

POINTS FROM LETTERS

Eradication of Malaria

Dr. R. B. HEISCH (Geneva) writes: In reply to the letter of my friend, Dr. L. J. Bruce-Chwatt (July 9, p. 150), I must point out that I did not state (June 4, p. 1736)—dogmatically or otherwise—that "malaria eradication in Africa should be carried out through the administration of anti-malarial drugs alone." I am merely anxious that anti-malarial drugs should be tried out on a large scale—that's all. If they fail—that's that.

Obituary

Sir ERNEST ROCK CARLING, LL.D., M.B.
F.R.C.P., F.R.C.S., F.F.R.

Few men in the medical profession have covered so diverse a field of activity as Sir Ernest Rock Carling, who died on July 15. As a surgeon he gained a reputation second to none, but apart from the work normal to a professional career he took a lead in the planning of the new Westminster Hospital and also established there a pioneer department of radiotherapeutics. His experience and authority in this subject involved him in innumerable advisory and administrative duties for the Radium Commission and King Edward's Hospital Fund and in service on special committes under three or four departments of State, the Medical Research Council, and other bodies. In the field of medical education he was an outstanding dean of his school and examiner in surgery to the Royal College of Surgeons and to a number of universities. He interested himself actively in the training of nurses, the service of almoners, and in social medicine, particularly in later years the care of the elderly. He was also concerned with the organization of health centres in the new towns, for example, Harlow in Essex. He was the author of many contributions to surgical textbooks. Yet it is not primarily for what he accomplished so conscientiously that those who knew him will remember him. They will recall chiefly an engaging personality, of untiring kindness combined with modesty and a striking capacity for self-effacement in the service of others.

[*Walter Stoneman, London*

Ernest Rock Carling was born at Guildford in 1877. At the age of 18 he went to Westminster Hospital as entrance scholar. In the intermediate M.B., London, examination he gained a gold medal and exhibition in pharmacology and therapeutics, and in the final M.B. (which he took in 1902) another gold medal and a scholarship, this time in obstetrics and gynaecology, so that already he gave indications not only of brilliance but of versatility. The B.S. he obtained in 1903. He had qualified M.R.C.S., L.R.C.P. in 1901, but before qualification he went out as a surgical dresser with the Imperial Yeomanry Field Hospital in the South African war, a useful experience for a young surgeon on the threshold of his career. Returning to Westminster, he held a house appointment in pathology, and then, on taking the F.R.C.S. in 1904, he became surgical registrar, and in 1906 reached the visiting staff as assistant surgeon. The first world war brought to him as to others a violent interruption in professional prosperity, but also an opportunity for the exhibition of sterling qualities. Rock Carling donned khaki for the second time and as captain in the R.A.M.C.,T. was mobilized at the outbreak of war and served the fourth London Hospital and in France and Flanders.

Many will recall the old Westminster Hospital opposite the Abbey. When Rock Carling went to the medical school as dean the hospital was ripe for reconstruction. He was one of those who wanted the hospital to remain on that splendid site and actually prepared plans for a new building there. It was eventually decided, however, to move to Horseferry Road to the south, and in 1930 he turned himself to what proved to be five years of labour in assisting to design a great new hospital, one of the most up-to-date and pleasant in the country. If buildings can absorb and retain something of the enthusiasm and ability which went into their planning and creation, then the spirit of Rock Carling is enshrined in the new Westminster. He was in all but the technical sense its architect. Before this, in 1928, with the aid of Mr. (now Sir) Stanford Cade, Dr. Flint, and one of his own two brilliant sons, Mr. Francis Carling, he designed the first and second radium "bombs" to be used therapeutically in this country, together with their container, and the famous radium annexe at Hampstead.

To radiotherapeutics Rock Carling made noteworthy contributions in various ways. In 1949 he was elected chairman of the Standing Cancer and Radiotherapy Advisory Committee under the National Health Service and was also chairman of the Clinical Subcommittee of the Medical Research Council concerned with the biological application of nuclear physics and consultant adviser, Atomic Energy Authority. He was chairman of the Therapeutic Uses Subcommittee under the Radioactive Substances Act, and a member of the Ministry of Labour's advisory panel on radioactive substances. He was chairman also of the International Commission on Radiological Protection. Soon after the outbreak of the second world war he was made honorary consultant to the Ministry of Pensions. He was also adviser on casualty services to the Ministry of Health and to the Civil Defence Department of the Home Office.

Carling served his own hospital, the Westminster, in an active capacity from 1906 to 1942. He was assistant surgeon until 1923, and surgeon from that year until his retirement at 65, under the age limit, when he became for the remainder of the war supernumerary surgeon. Later, until his death, he was consultant surgeon. The *Broadway*, under the easily identifiable initials of its then senior physician, said of him on his retirement from an active appointment that while nobody is indispensable there really is justification on occasion for the employment of that overworked and much abused adjective "unique," and that if it could be employed with regard to anybody it was "Rocky" Carling —"for it is impossible to replace him." The same writer said that whenever at Westminster an opinion was desired or an operation necessary the first name that sprang to mind was "Rocky," and no second name had ever been considered.

Among other hospitals which he served were the Seamen's Hospital, at Greenwich, the King Edward VII Convalescent Home for Officers, at Osborne, the Peace Memorial Hospital, at Watford, and the Chislehurst Hospital. In the field of medical education he was for many years a member of the Faculty and of the Board of Advanced Medical Studies of the University of London, and for ten years he was chairman of the Court of Examiners of the Royal College of Surgeons. He was also examiner in surgery for the universities of London, Edinburgh, and Sheffield, and examiner for the Faculty of Radiology. In the field of medical benevolence he was treasurer of the Society for the Relief of Widows and Orphans of Medical Men and a member of the Council of the Royal Medical Benevolent Fund. He was chairman of the Medical Advisory Committee as well as a trustee of the Nuffield Provincial Hospitals Trust, and chairman of the Committee of the Institute of Social Medicine at Oxford; also a member of the Medical Research Council and of the Radium Commission and Trust. In the Royal Society of Medicine he was president of the Section of Surgery in 1941–2, and in 1949 he received the honorary fellowship of the Society. This eminent surgeon had earlier been elected, in 1945, by the Fellows of the Royal College of Physicians of London to be one of themselves. In 1940 he had been made an honorary fellow of the Faculty of Radiology. He was president of the Medical Protection Society. His valuable work in many capacities was recognized by a knighthood in the Birthday Honours List for 1944. The honorary degree of LL.D. of Queen's University, Belfast, was conferred upon him in 1952.

He was joint editor (with Sir James Paterson Ross) of the many volumes of *British Surgical Practice*, joint editor of *British Practice in Radiotherapy*, editor of the *Course of Instruction in Radium Practice*, and author of many articles in medical journals and textbooks. His name will be found in such works as Walton's *Textbook of Surgical Diagnosis*, Choyce's *System of Surgery*, and Rolleston's *Encyclopedia*. In 1955 he delivered the Harben Lectures on "Ionizing Radiation and the Public Health." Our own columns, including those devoted to correspondence, have often been illuminated by his pointed contributions. He touched the work of the British Medical Association only at a few points, but he was a valuable member of the Fractures Committee set up by the Council in 1933, and he was vice-president of the Section of Surgery at the Annual Meeting at Bournemouth in 1934.

Sir Ernest Rock Carling married Petra, daughter of the late Rev. E. D. Rock, of Creeting St. Peter, Suffolk, and had two sons. Lady Carling died in January, 1959.

Sir CLEMENT PRICE THOMAS writes: Sir Ernest Rock Carling's death has removed from among us one of the surgeons to whom all looked up with respect and whom his many friends regarded also with great affection. He was one of those unique people who, having spent a busy life in one sphere, was able, after reaching the age of normal retirement, successfully to embark on another career of activity and service.

Sir Ernest's earlier life was spent chiefly in the Westminster Hospital. Here he started as a student, and subsequently, having been appointed to a staff vacancy which was created for him, he led the busy life of a surgeon, and was both teacher and friend to those fortunate enough to have been associated with him. His rather formal and judicial appearance covered a fund of warm humanity, only to be seen and fully appreciated by those who worked with him closely; to these he imparted his knowledge freely and easily, teaching as well from his failures as from his successes. He acted as arbiter for his colleagues and students alike. After his retirement from the staff he continued in his interest in all the hospital and student activities, giving up time which could be ill afforded from a life which was busier than before his retirement.

After he had retired the only changes were those of environment and of interest. Until a few years ago he worked 12 to 16 hours a day, and as often as not for seven days in the week. During the second period of his life his activities covered such interests as membership of the Atomic Energy Commission and chairmanship of the International Commission of Radiological Protection, membership of the Standing Advisory Committee on Cancer and Radiotherapy, and trusteeship of the Nuffield Provincial Hospitals Trust, to mention but a few of the things which claimed his interest and attention. There is no question that the second part of his life was the more rewarding, and without doubt it was the most valuable to the country at large. He took on a new lease of life and entered into this new sphere with all the dynamic energy which was so characteristic of him.

Ten years before he died he had the first signal of his fate, but undeterred he carried on as though that signal had never been received. In fact, during the last week of his life he attended a dinner in honour of one of his colleagues at which he made the principal speech, and he attended the meeting of his beloved Society of Widows and Orphans of Medical Men, of which he was treasurer for 40 years. On the day before his death he was present at his old hospital for the visit of the University Grants Committee.

He leaves behind him a host of friends and disciples who could do nothing better than try to emulate his example.

D. A. ABERNETHY, M.A., B.M., B.Ch.
F.R.C.S.Ed., M.R.C.O.G.

Mr. D. A. Abernethy, senior surgeon to the Radcliffe Infirmary and United Oxford Hospitals and lecturer in surgery to the University of Oxford, died on June 23 after a long illness. He was 62 years of age.

Douglas Allan Abernethy was born in London in 1898, the son of James Abernethy, a general practitioner in Barnes. He attended St. Paul's School, Hammersmith, where he held junior and senior scholarships. He went straight from school in 1916 into the Army and served in France and Belgium as a subaltern in the Royal Field Artillery until 1918, when he was severely wounded and invalided home. While convalescent he went up to Balliol College, Oxford, where he took second-class honours in natural philosophy (physiology) in 1922. He was awarded a half-blue for swimming and was in the university team for four years, becoming captain and president of the O.U. Swimming Club in his last year. He also gained a half-blue for boxing.

Abernethy pursued his clinical studies at St. Bartholomew's Hospital, and graduated B.M., B.Ch. in 1925. After six months as house-surgeon in gynaecology and midwifery at Bart's he returned to Oxford in 1926 to become house-surgeon at the Radcliffe Infirmary. In December of that year he was elected honorary assistant surgeon and surgical registrar to the Radcliffe Infirmary. He took the F.R.C.S. of Edinburgh in 1928 and was elected honorary surgeon to the Radcliffe in 1933. Here he worked for the rest of his life, becoming clinical lecturer in surgery to the university and also holding consultant appointments in various district hospitals. He was one of the pioneers in the work of blood transfusion at the Radcliffe, and was responsible for the introduction there of radium treatment.

F. K. B. writes: "Abers," as he was affectionately known both by his colleagues and his students, was one of the outstanding characters, in the best sense of the word, of the Radcliffe Infirmary. His natural consideration for others, his old-world politeness, and his gentle charm of manner were in keeping with his somewhat old-fashioned appearance. One thinks of him quietly puffing at his pipe under his moustache as he discussed the details of a case with one of his juniors, or sitting patiently in the surgeons' room waiting till his anaesthetist was ready for him, without any show of ill-humour even if the induction was protracted. As a general surgeon and a true artist he turned his hand to almost all types of work, but he preferred a small canvas when possible so that he could devote to it his meticulous and detailed care. He had a dislike of the heroic type of operation and was always mindful of what this sort of procedure might inflict upon the patient afterwards in terms of suffering without real lasting benefit. When in doubt about how far to go he would fall back on his practical common sense and human understanding, thus avoiding the pitfall of getting carried away by his own enthusiasm. This practical commonsense side of his character was also invaluable in committee and enabled him to cut through a mass of irrelevant material and get to the point.

Abernethy's firm was popular with students and residents, who found him an understanding teacher of sound basic principles without unnecessary frills and a sympathetic and experienced adviser when difficulties were discussed. His attitude when operating was characterized by courtesy to his assistants and the theatre staff, but he would not allow interruptions. "No messages are to be given to my house-surgeons till we have finished the operation," he would say, "since we can do nothing about it and it only worries us—unless," he would add, "it is an invitation for him to go out to dinner." Outside his professional life he had very wide interests. Apart from swimming he was keen on other open-air activities. In his younger days he enjoyed horse-riding, and when honorary surgeon at the Radcliffe he was a member of a small group holding a rough shoot in the country near by. But his main love was for trout fishing, at which he was adept. He would time part of his annual holiday to coincide with the appearance of the May-fly, about whose habits he had a most profound knowledge based on carefully kept notes of personal observations extending back for years.

Douglas Abernethy was interested in all branches of science, in literature, and in the arts, and he appeared to know something about everything. For the past thirteen years he had been secretary and moving spirit of the Oxford Medical Club, where papers on non-medical subjects were read, and here his gifts as an erudite speaker on any and every subject were shown to perfection. He was a connoisseur of good food and wine, and an excellent cook. His skill in practical handiwork, including metalwork and cabinet-making, was outstanding. Among other things, he built several violins of great beauty and reconstructed an early piano of about 1830 vintage, in a deplorable condition, rescued from a village shed; he made it function again as a lively old instrument.

During his last illness he showed an amazingly patient and courageous outlook on his trouble, discussing dispassionately and in detail the various stages with his friends and not shying at its worst aspects. He recited to the writer a beautiful and delicate flower poem he had composed very shortly before his death. A very remarkable and charming personality has been removed from us. He is survived by his wife, a son, and a daughter.

C. J. THOMAS, B.Sc., M.B., M.R.C.S., L.R.C.P. D.P.H.

Dr. C. J. Thomas, at one time a senior medical officer to the London County Council, died at Acton on June 30. He was 84 years of age.

Charles James Thomas was the last survivor of the trio who founded the London School Health Service in the first decade of this century. The others were Drs. James Kerr and F. C. Shrubsall. Thomas took a degree in science in 1894, and at the London M.B. examination in 1901 he was awarded a gold medal in medicine and obstetrics. He was trained at St. Bartholomew's Hospital and held house appointments there and at the Hospital for Sick Children, Great Ormond Street. His first major work for the London County Council was to report in 1908 on an epidemic of measles in Woolwich. Later he made a study of the reasons why children were absent from school for long periods. He discovered that acute rheumatism was the main cause, and inaugurated the London rheumatism scheme to help to prevent rheumatic heart disease. He also took an active part in the provision of open-air schools for debilitated children.

His outstanding qualities ensured that Thomas rose rapidly in the L.C.C. hierarchy, and he was senior medical officer in charge of the school medical service, as it was then called, for almost a generation. He believed in part-time service, and attracted to his division many paediatricians who are now leaders in that specialty. He would recite their names with great pride.

At the outbreak of the first world war Thomas was in Germany on holiday and was interned in a hotel for a few weeks until he was exchanged for a German doctor. He said that he was the only person present in the crowd before the Kaiser's palace when war was declared and in the crowd before Buckingham Palace when it ended. He was responsible for the medical arrangements when many thousands of London schoolchildren were gathered from all parts of the county to view the coronation procession of King George VI, and he received the Coronation Medal for his services on this occasion.

He was due to retire soon after the second world war began, but was kept on to help to solve the many difficult problems arising out of the evacuation of London schoolchildren into safer areas. He slept during the bombing in a cellar of County Hall. He always slept well despite the intensity of the "noises off," because he removed his hearing-aid and never heard a sound. Despite his deafness for

ordinary conversation he could, with his aid, hear music, and one of his recreations was to listen to gramophone records.

Though it often involved toil well into the night, he always produced the draft of the annual report of the school medical service by the end of February. His reports were invariably accepted without alteration and are storehouses of achievement and wisdom.

Thomas was a most remarkable man: genial, of the highest intellectual integrity, a friend of all his staff, and a man in whom his committees had the greatest confidence.

Sir Gwilym Gibbon, in his book on the jubilee of the L.C.C. written in 1939, wrote of the London school health service: "There is cause here for great pride." Thomas had no personal pride save in the achievements of his children and his staff, but he is the man who made pride in the London school health service possible.—A. D.

C. W. J. I. writes: The news of the death of Dr. C. J. Thomas was received with heartfelt regret by his many friends and colleagues, not only those who lived and worked with him in the service of the L.C.C. but also by a much larger circle of men and women whose interests lay in the field of preventive medicine and in particular in the welfare of London schoolchildren.

During the whole of his career Dr. Thomas was connected with the school medical service of London. On its reorganization in 1911 he assumed direct responsibility for the administration of the revised arrangements under the school medical officer. The success of his work is seen not only in the vastness and efficiency of the London school health service to-day but also, what would be much more important to Thomas, in the immense improvement in the health and well-being of the London schoolchild compared with the pioneering days preceding the first world war.

Outside his official life Dr. Thomas had many interests. He played Rugby for Wales in his early days, and in later years his chief recreations were philately, fishing, and gramophone music. He was married and had five children, and was a typical example of a happy family man. He reflected this side of his character in his dealings with the numerous junior members of the medical staff of his department, and any officer—medical or lay—who was in need of advice or sympathy in his or her personal life was always sure of a ready hearing, sound advice, and sympathy, sometimes even to the shedding of common tears with the senior medical officer. It is this human side of Dr. Thomas's character which will always be remembered best in the hearts of those of us who had the privilege of working close to him in the long years of his service with London's schoolchildren.

ALEXANDER KENNEDY, M.D., F.R.C.P., D.P.M.

The obituary of Professor Alexander Kennedy was published in the *Journal* of June 25 (p. 1960).

W. M.-G. writes: I would like to contribute a word of sorrow and praise because, like so many others, I feel Kennedy's untimely death a great loss to British psychiatry. His sudden and most unexpected departure was due to a cardiac infarction of which an earlier warning had happened a year before. He remained true to his "condottieri" nature until his last breath; but specialties such as psychiatry struggling for recognition are so much in need of brave fighters of his kind, defending their field and counteracting the take-over bids of other branches of medicine. Kennedy saw these dangers clearly, and when he linked up with medicine he did not do so in order to dissolve psychiatry in favour of the big brother. Although he considered himself versed in the skills of a great politician, he was a most reliable comrade-in-arms in all good causes. His brilliant, penetrating intellect was seen in everything he endeavoured, and in spite of his temperamental impatience he thought out original and independent solutions of whatever he touched: planning of psychiatric services in Australia; German rehabilitation in the post-war period; power struggles in Egypt; instruction of the general public on psychiatric questions; link-up of mental hospital psychiatry with the university department and chair; and so on. Just when he was able to begin to harvest some of his fruits in Edinburgh he had to go, leaving an example for the younger generation difficult to emulate and a gap which will be equally difficult to fill.

Medical Notes in Parliament

RADIOACTIVE FALL-OUT AND SCHOOL-CHILDREN'S MILK

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Lord TAYLOR received from Viscount Hailsham, Lord Privy Seal and Minister for Science, on July 14, a specific assurance that the consumption of milk among school-children had not been adversely affected by publicity given to the effects of radioactive fall-out. No representations, Viscount HAILSHAM said, had been received from local education authorities to the effect that it had. Any decrease in the consumption of milk was attributable to the increased numbers of children in secondary schools, where the amount of milk drunk was normally lower than in primary schools. He agreed with the view expressed by Lord Taylor that it would be a thousand pities if there were any decrease in consumption because people were unjustifiably frightened that the milk would harm their children in some way. Lord TAYLOR'S opinion was that the danger of not taking milk was far greater than the danger of doing so.

Leukaemia in Wales and Cumberland

But the two speeches that were hung on this peg ranged considerably wider. Lord Taylor referred to the increase of strontium-90 in the diet—particularly in milk, and in the bones of new-born children—of which reports began in 1958. It appeared to be coming from radioactive fall-out, and was brought down by rain. The peak was reached between March and June, 1959, almost certainly as the result of fall-out from the large series of Russian atomic tests in 1958—just before the ban on atom bomb testing—and he asked for confirmation that the figures were now starting to fall. One point that had worried serious medical scientists was the steady increase over the past 20 or 30 years in leukaemia, particularly the extraordinary increase in some counties in Wales and in Cumberland, which now caused about five deaths per 100,000 of the population every year, mainly in infants and old people. Dr. Phillips, medical officer in South Caernarvonshire, had found that there had been a 50% increase in the four hill counties of Wales and in Cumberland. It was tempting to conclude, Lord TAYLOR said, that there was some relationship between this and the increase in the fall-out of strontium-90 in those areas. But he was convinced this could not be so, for the quantity of strontium-90 was so minute that it was not enough to produce this effect.

There must be a reason for it, and he hazarded the guess that a much more likely cause was increased diagnostic radiology. Since the coming of the National Health Service there had been a tremendous improvement in *x*-ray services. It was much more likely that increased diagnostic radiology in these backward counties explained the increase in leukaemia, because they were now coming up to the level of the more forward counties. Strontium-90 was far less important than diagnostic radiology, in his view, as a source of radiation. It would be far more important to be extremely stringent in regard to unnecessary *x*-rays than in the consumption of milk. *X* rays were often insisted on in courts of law; that was why a great many unnecessary *x* rays were taken by doctors, and he thought that views on that would have to be revised.

Radioactivity Reports Due in September

Viscount HAILSHAM was not briefed on this occasion to explain the rise in leukaemia, but offered one comment—having asked the same question—from his advisers that the absolute figures were so small, although the percentage rate seemed large, that the increase could really be without final significance. On the general issue, he said it had been Government policy to give all the reliable information that they could to enlighten and instruct public opinion; and he declared emphatically that they had suppressed absolutely nothing, and had not sought to influence the scientists in any way in the advice they had given. Some irresponsible comment had gone so far as to suggest that reports from the Medical Research Council's panel had in some way been influenced by the Government. As the one member of the Government who could have influenced, he gave a categorical denial that it had been done.

The monitoring service carried out mainly under the responsibility of the Agricultural Research Council, with the assistance of experts from the Medical Research Council, was generally accepted as better than any other nation had available. Another report was almost due, and would be published about September. Another report was also due from the panel of experts convened by the M.R.C., and he hoped it would be published about the same time. Their reports had always been unanimous, and were completely uninfluenced by any consideration of policy whatever, except to provide the scientific truth. He answered Lord Taylor's request for confirmation about the decline in radioactive fall-out with the statement that the next monitoring report would tend to show the increase in fall-out due, in the main, to the Russian tests at the end of 1958 leading to a rapidly increased fall-out which reached its peak in March, 1959. Thereafter, and in the latter part of 1959, the report would show a rapid falling off, which would continue unless the unhappy event occurred of "someone letting off another of these things in the atmosphere." The Government wished to see an end of these tests.

QUESTIONS IN THE COMMONS

Doctors' Anonymity in Out-patients

Mr. WILLIAM GRIFFITHS (Manchester, Exchange, Lab.) asked the Minister of Health on July 11 whether he would instruct the Manchester Regional Hospital Board and the Governors of the United Manchester Hospitals to take action in all out-patient clinics in hospitals under their control to make the patients aware of the identity of the doctors who saw them at the clinic. Miss EDITH PITT, the Parliamentary Secretary, replied that this was a matter for hospital authorities themselves to decide, in consultation with their medical staff.

Mr. GRIFFITHS asked her if it was not undesirable that people who thought they would get the opinion of a consultant often did not see him—although there might be good reasons for that. What was even worse was that they had no idea who saw them. They were entitled to know who was examining them. The initiative should come from the Ministry. The Parliamentary Secretary was passing the buck. Miss PITT said that when the general practitioner named a consultant in the letter brought by the patient, normally that consultant would see the patient. Mr. GRIFFITHS interjected—That is not true at all. Miss PITT, continuing, added that to conserve time his opinion might be conveyed in a letter from the registrar to the practitioner. She also said that in her own experience with members of her family they had seen the consultant, and she would expect to find that to be general. She hoped that Mr. Griffiths's question would bring the matter to the attention of the regional hospital board, which was the proper authority.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) said the Ministry should make it clear to hospitals that they did not wish doctors always to wear a cloak of anonymity. "The time has come when consultants must be told," she said, "that they have no right under certain circumstances to allow their registrars to deputize for them. On the whole, most of them do very fine work, but there is some evidence that there is too much deputizing in some hospitals." Miss PITT replied that there were occasions when a new patient might better be seen in the first instance by a registrar, for history taking and preliminary tests, but the final responsibility rested always with the consultant. That was the point on which she wanted to reassure M.P.s.

Waiting Time in Hospitals

The SECRETARY OF STATE FOR SCOTLAND told Mr. W. Hannan (Glasgow, Maryhill, Lab.) on July 12 that he had received the reports from hospitals about waiting times in out-patient departments, and they were being studied. Mr. HANNAN said there was a growing volume of complaints from out-patients, and indeed from some doctors, about the frustration and time lost in waiting, and he asked for early publication of the results of the survey. Mr. J. S. MACLAY replied that he was aware of the importance of the problem. He would have to consider whether the full reports could be published, and whether they were in a form that made that possible.

Why November for Mental Health Act

The decision to bring the local authority services section of the Mental Health Act into operation on July 15, and the remainder of the Act on November 1, was reported in the *Journal* last week (p. 240). When the announcement was made by the Minister of Health on July 11, Mr. KENNETH ROBINSON (St. Pancras North, Lab.) welcomed the co-operation that the Minister and the department had given to the Mental Health Year, and the implementation of parts of the Act immediately, but asked what was the delay in implementing the remainder. Mr. WALKER-SMITH gave him two reasons. First, hospitals and local authorities must be given sufficient notice to familiarize themselves with the advice in circulars, which would be lengthy. Second, certain preparatory action had to be taken by the local authorities. As they were not very active during August and September it had been necessary to fix the date for November 1.

The Minister added in reply to Sir H. LUCAS-TOOTH (Hendon, South, Con.) that the chairman of the 15 regional mental health review tribunals were to be appointed with effect from August 1. The tribunals would be in operation when the main part of the Act came into force on November 1, from which date applications from patients could be received.

Mrs. E. BRADDOCK (Liverpool, Exchange, Lab.) asked the Minister to make certain that no patient was discharged from hospital until the local authorities had the necessary services to accept them. She said that in some areas there was already friction between the hospitals and local authorities because the hospital authorities insisted on discharging patients without consultation with the local authorities. Mr. WALKER-SMITH agreed that it was vitally important that there should be close liaison between the hospital authorities and local health authorities.

Kent Proposal for Residential Accommodation

Mr. N. DODDS (Erith and Crayford, Lab.) was told that the proposals of the Kent County Council had been approved for the provision of residential accommodation for patients who could leave mental hospitals but for the fact that they had nowhere else to go. Mr. DODDS asked if the Minister was satisfied that because of these proposals many of these patients could look forward with hope to getting their liberty, or were the proposals very restrictive? Mr. WALKER-SMITH said the county council undertook in its proposals to provide residential accommodation for this class of case, but the priority in which it included projects in its building programme was a matter for the council.

Medico-Legal

MANSLAUGHTER OF MONGOL CHILD

[FROM OUR LEGAL CORRESPONDENT]

At the Surrey Assizes at Kingston-on-Thames on July 1, Major George Ernest Johnson, aged 40, of the Royal Corps of Signals, was convicted of the manslaughter of his 3-month-old mongol child and sentenced to 12 months' imprisonment. Major Johnson was acquitted of murder (*The Times*, July 2).

After learning from his doctor that his son was a mongol child, Major Johnson brooded on the matter, and finally killed the child by placing a gas-poker in his cot after baptizing him. The defence put forward on Major Johnson's behalf was that at the time of the killing his mind was so tortured that his responsibility for the act was substantially impaired within the meaning of Section 2 of the Homicide Act, 1957.

In summing-up to the jury, Mr. Justice Slade directed them that there was no evidence that Major Johnson was insane, and no evidence that the killing was other than unlawful. The only possible defence to the charge of murder was diminished responsibility. In passing sentence, Mr. Justice Slade said that he took into account Major Johnson's motives of compassion and his good character and unselfishness, but on the other hand he had to consider the fact that the killing was committed knowingly and after considerable premeditation. "I cannot pass over a matter of that gravity resulting in the death of this child, lest other people might be tempted to think they can deal in this way with any mongol child, misformed child, or child not in possession of his faculties."

DISABILITY AND DRIVING

[FROM OUR LEGAL CORRESPONDENT]

Three recent prosecutions in driving cases raised questions of physical disability in different ways.

Hypoglycaemic Attack

The first of these cases concerned a fitter and welder who was a diabetic. On April 15 he pleaded guilty before the Wonford magistrates to driving a car without due care and attention (*Western Morning News*, April 16). He had been a diabetic for 23 years and had been driving since 1943 without any previous difficulties, but on the occasion in question he was involved in a collision while driving on the wrong side of the road: after the crash he was found slumped in the driving seat with little awareness of what had occurred. In mitigation it was said that he was at the time late for his midday meal and unknown to him his insulin dosage was incorrect; at the time of the accident, when he was a mile from home, he was feeling drowsy. He was fined £10 and his licence was endorsed: he was told by the Bench that he ought to have stopped driving when he felt drowsy.

Post-epileptic Automatism

In the second case an acquittal was secured on the rare ground of automatism. A factory worker, aged 49, was acquitted by the Oxford magistrates of a charge of dangerous driving on April 12 (*Daily Telegraph*, April 13). He had driven into Oxford at 40 m.p.h., and hit the rear nearside of another car, and had overtaken it on its nearside. He had then gone to the offside and collided with a police motor-cyclist, struck a number of other vehicles and a pedestrian, and only stopped after wrecking a traffic signal control box at Carfax. He pleaded not guilty, on the ground of automatism, saying that he remembered nothing of the collisions. He had had two head injuries, one in 1929 and the other in 1934, when he was unconscious for several weeks. He had not had any blackouts since. Dr. H. D. Leggat, who examined him after the accident, said that there was no abnormality, but agreed that the circumstances could have been consistent with an attack of petit mal. Dr. J. M. K. Spalding, neurologist, said he was satisfied that the defendant suffered from epilepsy and that the accidents occurred during a major attack: since then he had suffered two minor attacks: the onset of epilepsy at this age was a recognized phenomenon. In evidence, the defendant said he had now handed his driving licence to his solicitor pending instruction from the licensing authority.

Under Section 5 of the Road Traffic Act, 1930, if a licensing authority is satisfied that the holder of a driving licence is suffering from any of certain specified diseases or disabilities (including epilepsy), or from any other disease or disability which would be likely to cause the driving of a motor vehicle by him to be a source of danger to the public, they may revoke the licence, subject to an appeal to the magistrates' court.

Deaf and Dumb Driver

The rules in the same Section concerning application for a licence were referred to in a third case concerning a deaf-and-dumb driver. On application for a driving licence, the applicant must declare whether he is suffering from any of the specified diseases or disabilities (which do not include deafness) or from any other disease or disability which would be likely to cause the driving of a motor vehicle by him to be a source of danger to the public. The National Institute for the Deaf advise their members to answer "No" to this general question, in respect of their deafness. It appears that there is no reported decision whether or not deafness does fall within this general class of disabilities likely to give rise to a source of danger, and the question was not strictly in point in this prosecution. The prosecution was brought against a deaf-and-dumb dental mechanic, aged 26, for failing to stop at traffic lights and driving without "L" plates and without a qualified driver. In respect of those offences, the Bath magistrates imposed disqualification from driving for 50 years and fines totalling £6. Clearly, in imposing this punishment, the magistrates had taken into account the irrelevant factor of the defendant's deafness. On appeal to the Bath Quarter Sessions on April 10 (*The Times*, April 11) the disqualification was reduced to four months.

RADIONICS AND THE BLACK BOX

On July 18 Mr. Justice Davies gave judgment for the defendant in the action for damages for fraud brought by Miss Catherine Olivia Philips, of Porlock, against Mr. George Walter de la Warr, of Oxford (*Journal*, July 9, p. 156; July 16, p. 241). His Lordship directed that since the plaintiff was a legally aided litigant with a nil contribution there should be no order for costs unless a further order is made. The judgment will be summarized in this column next week.

CORONERS' CASES

Fractured Skull Simulating Drunkenness

James Albert Groves, of St. Paul's, Bristol, died of a fractured skull two days after he had been admitted to hospital. At a Bristol inquest a jury returned a verdict that death was due to an accidental fall. Evidence was given that the deceased had consumed two pints of cider and one of beer during the evening. Two witnesses said he was sober on leaving the public house, and his wife said he was accustomed to cider and was never the worse for drink. He was later found by a policeman lying on the ground. On being lifted up he mumbled that he was all right and acknowledged that he had "had a couple." Because he was incoherent and smelt slightly of drink the officer came to the conclusion he was under the influence of alcohol. Groves turned and went on his way rather unsteadily and was later found by two more officers lying on the ground. They formed the same opinion of his condition and they helped him behind a wooden hoarding and left him to "sleep it off." One of the officers concerned said in evidence that there were not enough policemen to arrest

every drunk. It was the practice in the docks to allow drunks, particularly seamen, to sleep off the effects of drink.

The deceased was later removed to hospital, where he died after two days from a fractured skull. There was no evidence as to how he came by this injury, and the Bristol coroner, Mr. J. A. Seymour Williams, recorded the jury's verdict that death was due to a fractured skull consequent upon an accidental fall (*The Times*, June 1).

Universities and Colleges

UNIVERSITY OF GLASGOW

On June 25 the degree of Ph.D. was conferred on F. H. Leckie, L.R.C.P.&S.Ed., M.R.C.O.G.

UNIVERSITY OF ABERDEEN

Dr. J. A. M. Findlay has been appointed to a terminable Lectureship in Anatomy, and Dr. G. M. Robb as Assistant in Biological Chemistry, both from October 1, 1960.

UNIVERSITY OF EDINBURGH

At a meeting of the University Court on June 20 honorary status was conferred as follows: Dr. David Ross, Honorary Senior Lecturer in Psychological Medicine; Dr. J. D. Haldane, Honorary Lecturer in Child Psychiatry; and Dr. A. D. Forrest, Honorary Lecturer in Psychological Medicine.

Dr. J. H. Turner was appointed assistant in the Department of Pathology.

Dr. J. S. Munro resigned from his appointment as part-time Lecturer in the General Practice Teaching Unit on June 30, and Dr. A. G. C. Renwick resigns from his appointment as Lecturer in the Department of Bacteriology on August 31.

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

The following degrees were conferred on June 30:

M.D.—Eunice Hurworth, I. J. Temperley.

M.A.O.—J. H. N. Ferris.

M.B., B.Ch., B.A.O.—D. Abrahamson, R. C. Barton, A. Clements, T. F. Conneen, Margaret B. Darley, J. Dolan, D. B. Dunham, Mary E. Elland, D. M. Gabbé, Mariana Goulandris, I. D. Grieve, J. F. A. Harbison, Wendy P. Holmes, Kathleen G. Llewellyn-Jones, Isabella V. Lalsingh, J. N. Lavan, G. C. A. Lemon, Mary S. E. McElroy, W. H. A. MacMahon, D. G. Martin, A. A. P. Meeson, Joy L. Nicholas, C. S. Norman, D. S. Nowlan, R. H. O'Connor, Katharine J. Sheehan, R. C. Simpson, I. Slater, Edna V. Sleith, S. G. Smith, B. J. Spencer, J. H. Thompson, A. Tomkin, R. T. Wales, S. C. Woko.

UNIVERSITY OF LONDON

The degree of M.S. was awarded to F. G. Ellis on May 18 and the degree of M.D. to P. O'Gorman and B. Ll. C. Phillips on May 25.

The degree of Ph.D. in the Faculty of Medicine was awarded to N. Marks (Institute of Psychiatry) on May 10 and to M. A. Crawford (Postgraduate Medical School of London), F. A. Hosni (Institute of Ophthalmology), and J. F. A. P. Miller (Institute of Cancer Research: Royal Cancer Hospital) on May 25.

The title of Reader in Growth and Development of Children has been conferred on Dr. J. M. Tanner in respect of his post at the Institute of Child Health.

The University has instituted an M.Sc. degree in Radiation Biology and Radiation Physics for candidates registering in and after October, 1960. Copies of the regulations for the degree and other details can be obtained on application to the Academic Registrar, University of London, Senate House, London, W.C.1.

UNIVERSITY OF MANCHESTER

The following candidates have satisfied the examiners at the examinations indicated:

CH.M.—M. Fox.

FINAL M.B., CH.B.—[1 2 3]A. E. H. Emery, [1 4]E. Jackson, [1 4]A. S. Tavill, J. H. Ainsworth, Valerie Anderson, R. A. Appleton, A. Barabas, Rosemary Barnes, P. Bee, B. Benster, M. M. Bluck, Maureen T. Boland, C. M. Bowkett, A. B. Brown, D. B. Clements, Claire Connors (née Tapper), J. L. Craven, A. C. Crompton, A. J. Crook, J. H. Earnshaw, G. A. Eccleston, Heather C. Ellwood, A. E. Fishburn, A. Garner, G. R. Giles, J. A. Glass, M. Gringras, S. G. Hammersley, A. W. Hargreaves, J. B. Hobson, J. Hodgkins, Jean M. Horrobin, T. Hughes, G. Ingram, S. M. Jackson, [2]S. Jowaheer, M. F. Kilshaw, J. O. Lee, M. D. Lee, Anne K. Lumb, M. J. MacCulloch, Sylvia Manton, L. A. Michael, M. L. Neale, Margaret H. Ogden, R. S. Parker, H. V. Penketh, H. E. Porte, Pamela Proctor, G. N. Radcliffe, F. H. Ratcliffe, J. Rhodes, D. I. Rushton, M. E. Serjeant, Mary S. Smith, Joan E. Speight, W. G. Staff, Jill Taylor, E. H. Thomas, J. Tinker, Annie S. Tomlinson, M. R. Whittaker, Marian Whitwham (née Box), Margaret Wood, Jeanne M. Wright.

DIPLOMA IN PUBLIC HEALTH.—G. R. Brackenridge, E. J. H. Foster, B. Gilbert, F. P. Peach, Beryl L. Sephton, A. Sippert.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—*Part I*: B. D. Hughes, Moira P. Jonas (née Dillon), G. Sedman, M. Segal. *Part II*: J. Devlin, Constance M. Duddle.

[1]With honours. [2]Distinction in obstetrics and gynaecology. [3]Distinction in medicine. [4]Distinction in surgery.

UNIVERSITY OF WALES

WELSH NATIONAL SCHOOL OF MEDICINE

The following candidates have been approved at the examination indicated:

M.B., B.CH.—[1 2 3 4 5 6 7]A. D. Griffiths, Margaretta E. Addis, D. Banks, J. D. M. Blayney, A. R. Boyns, [8]P. M. Brown, [8]G. Crompton, [4]T. G. Davies, B. D. Dennis, A. B. Dew, P. J. Edwards, Eryl C. Evans, Patricia M. Ford, [4]L. Gable, Mair E. Gibbs, J. C. Gingell, E. F. Griffith, D. J. L. Hughes, [5 6 7]Celia F. K. Jeffery, C. K. Jones, H. H. G. Jones, [5 8 9]J. G. Jones, K. H. Jones, J. B. Miles, S. Nam, E. R. Norton, Margaret V. Poultney, Jean E. McK. Thomas, [3 4]P. Valabhji, [4]C. W. Vellani, P. Wentworth, Anne M. Williams, D. M. J. Williams, K. Woodbridge, D. Worgan.

[1]With honours. [2]Distinction in Human Anatomy. [3]Distinction in Physiology. [4]Distinction in Pharmacology and Therapeutics. [5]Distinction in Surgery. [6]Distinction in Medicine (including Psychological Medicine). [7]Distinction in Child Health. [8]Distinction in Social Medicine and Public Health. [9]Distinction in Midwifery and Gynaecology.

UNIVERSITY OF BIRMINGHAM

The following appointments are announced: Dr. J. H. Bulmer, Dr. A. Rhodes, Dr. J. Steinhert, and Dr. N. G. Lambert, as temporary Lecturers in the Department of Anatomy; Dr. N. Segal as temporary Lecturer in the Department of Medicine; Mr. G. D. Oates as temporary Lecturer in the Department of Surgery.

Sir Arthur Thomson has been reappointed representative of the University on the Inter-university Council for Higher Education Overseas.

The title of University Research Fellow has been given to Dr. P. J. Jeavons, honorary senior research associate in paediatrics in the United Birmingham Hospitals and consultant psychiatrist, All Saints' Hospital, Birmingham, during the tenure of his present appointment in the Department of Paediatrics and Child Health.

The board of governors of the United Birmingham Hospitals have granted honorary status to the following members of staff: Dr. R. F. Fletcher (Honorary Senior Registrar in Medicine); Mr. J. A. Williams (Honorary Senior Registrar in Surgery); Dr. Sylvia J. Darke (Honorary Research Associate in Experimental Pathology).

Dr. D. R. MacMillan has been appointed Research Fellow in the Department of Paediatrics and Child Health for one year from July 11, 1960.

UNIVERSITY OF LEEDS

The following candidates have been approved at the examinations indicated:

CH.M.—C. R. Berkin (with distinction).

M.B., CH.B.—E. O. Amaku, A. A. Azulay, F. Bostock, Eileen M. Brocklehurst, J. G. E. Bruce, J. R. Cole, Anne E. Cooke, Sylvia Dennison, R. Franklin, D. L. Hanson, B. J. Kirby, J. P. Lakins, J. K. Shepherd, Myra J. Wigoder, A. S. Wotherspoon.

UNIVERSITY OF BRISTOL

The following candidates have been approved at the examinations indicated:

M.B., CH.B.—[1]T. F. Draisey, [1 2]D. R. Ferguson, [1 3]Margaret E. Marsh, [1 2]Jean L. Morley, [1]Barbara M. Morris, [1 3 4]G. Neale, [1]N. H. Stentiford, J. B. Beddard, Barbara A. Beesley, Margaret J. Bisson, P. G. Bisson, A. G. Blandford, R. J. Clarke, P. H. Cottrill, Sheila A. Critchley, A. R. Daniel, C. Dyall, T. H. Flaherty, M. J. Gay, B. J. Gorman, P. W. V. Gurney, B. W. Hackman, C. J. Hayward, A. Hinchliffe, A. G. S. Langley, Isobel C. Malkin, Mary P. Miles, R. H. Pitman, Isabel M. S. Price, J. C. D. Rawlins, W. J. C. C. Rich, J. N. Sebire, P. H. Taylor, D. P. Warnecke, R. J. Whatley, D. M. D. White, B. E. O. Williams, J. R. Winslade. *In Group I completing the examination*: M. G. Dash.

DIPLOMA IN PUBLIC HEALTH.—S. Addis, J. R. Blancarte, Z. J. Brzezinski, Christina F. J. Ducksbury, Marjorie Mair, C. M. McGregor, I. O. Osman, R. Y. Taylor.

[1]With second-class honours. [2]Distinction in Surgery. [3]Distinction in Public Health. [4]Distinction in Child Health.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

The following candidates, who were successful at the recent Conjoint final examinations, were admitted in June to the Licence in Medicine and Midwifery: A. Bianchi, P. E. Buckeridge, A. P. Brennan, P. M. C. Chan, R. Chen, M. Coovadia, A. I. Dangor, G. K. Darby, S. D. Dervish, Shiu-Cheong V. Fok, P. D. B. Forsythe, Doom-Raz Gaya, A. H. Goldberg, A. J. Gomes, L. A. G. Greene, A. K. P. Harbison, C. A. Harkin, J. E. B. Hannigan, N. M. Hogan, T. G. Hogan, J. T. Iwanowska, S. MacD. Johnson, F. C. Keshavjee, H. C. R. M. Kilgallen, K. Kumarashwaran, Lor Kai Hung, M. S. Mather, W. G. A. Maxwell, F. T. A. C. Murphy, J. V. M. McGrath, Ng Jit Leong,

M. I. O'Boyle, G. J. O'Connor, K. A. Qasem, D. S. Rustomjee, K. Sayed, S. Selvendra, C. B. Short, H. B. A. Somarantne, D. E. Suleman, W. E. Swiecicka, B. M. Taaffe, K. K. Tan, M. A. I. Tansey, Tay Beng-Choo, G. L. K. Tong, S. K. Verma, M. B. P. Whelan, Kwo-Wee Yu.

ROYAL COLLEGE OF SURGEONS IN IRELAND

On June 24 the Licence in Midwifery and Surgery of the College was conferred on the following candidates:

Angeliki Bianchi, Pauline E. Buckeridge, A. P. Brennan, P. Min Chung Chan, R. Chen, Moosa Coovadia, A. I. Dangor, G. K. Darby, Sheila D. Dervish, Shiu-Cheong Vincent Fok, P. D. B. Forsythe, Doom-Ras Gaya, A. H. Goldberg, A. J. Gomes, Lorna A. G. Greene, Alexandra K. P. Harbison, C. A. Harkin, Joan E. B. Hannigan, Nuala M. Hogan, T. G. Hogan, Jadwiga T. Iwanowska, Sheila MacD. Johnson, Fatehalli C. Keshavjee, Helen C. R. M. Kilgallen, K. Kumarashwaran, Lor Kai-Hung, M. S. Mather, W. G. A. Maxwell, F. T. A. C. Murphy, J. V. M. McGrath, Ng Jit Leong, M. I. O'Boyle, G. J. O'Connor, Clare B. Short, K. A. Qasem, D. S. Rustomjee, K. Sayed, S. Selvendra, H. B. A. Somaratne, Dulci E. Suleman, Wanda E. Swiecicka, Brigid M. Taaffe, Khim Keng Tan, Tay Beng-Choo, Gloria Lai-Kit Tong, S. K. Verma, Mary B. P. Whelan, Kwo Wei Yu.

At a meeting held at the College on July 8 the President, Mr. T. G. Wilson, inaugurated the new Faculty of Anaesthetists. The following are the members of the first Board of the Faculty: *Dean*, Dr. T. J. Gilmartin; *Vice-Dean*, Dr. V. O. McCormick; *Honorary Secretary*, Dr. J. A. Woodcock; and Dr. P. J. Drury Byrne, Dr. Ethel Sheila Kenny, Dr. P. F. Murray, Dr. G. R. Davys, Dr J. W. Dundee, and Dr. S. H. S. Love.

In addition to the Board members, the President also admitted the following as Foundation Fellows: Dr. S. N. Basu, Dr. Kathleen Bayne, Dr. W. Bingham, Dr. J. Boyd, Dr. G. J. C. Brittain, Dr. D. G. Coleman, Dr. W. S. Davis, Dr. S. Margaret E. Deane-Oliver, Dr. K. B. Glynn, Dr. T. F. Heavey, Dr. J. C. Hewitt, Dr. Margaret M. V. Lemon, Dr. J. A. Macaulay, Dr. Mary J. A. O'Connor, Lady (Frances Edna) Read, Dr. R. W. Shaw, and Dr. M. A. Woods. *In absentia:* Dr. J. D. Bourke, Dr. A. B. Bull, Lieutenant-Colonel F. MacD. Byrn, Dr. A. H. Kasasian, Professor O. V. S. Kok, Dr. Z. Lett, Dr. B. V. Lyne, Dr. P. R. Mesham, Dr. Maureen Murphy, and Dr. D. L. Scott.

The honorary Fellowship in the Faculty was conferred by the President of the College on Dr. John Gillies and Dr. G. S. W. Organe.

Vital Statistics

Lymphocytic Meningitis at Cardiff

An outbreak of lymphocytic meningitis has so far affected 70 persons, mostly children, in and around Cardiff. No deaths have occurred. We are indebted to Dr. G. EMRYS HARRIES, consultant in infectious diseases at the Lansdowne Hospital, for the following information.

Since the week ending May 6, up to 12 cases a week have been admitted to hospital. The cause of the disease is probably a non-specific virus, which is still being investigated. The ages of the patients are as follows:

Age in Years of Patients

	1–4	5–9	10–14	15+	Total
Male	10	19	7	10	46
Female ..	4	8	2	10	24
Total ..	14	27	9	20	70

Among those patients aged 15 and over, six were between 25 and 40 and two men were 59 years of age. Twice as many male cases as female were admitted. In only three families were there two cases from each.

In most cases the temperature rose to 103° F. (39.4° C.) or more, and pulse rates were raised. The signs and symptoms are headache—mainly frontal—vomiting, neck stiffness, positive Kernig's sign, stiffness of limbs, and often lethargy for the first few days. Photophobia is rather common. On lumbar puncture the cerebrospinal fluid showed: globulin, increased; leucocytes, mainly raised to 40–800 (chiefly lymphocytes) but a few cases showed 1,000 per c.mm.; sugar, normal; no organisms seen. The finding of normal sugar rules out cerebrospinal fever and tuberculous meningitis. The average stay in hospital has been three weeks, with symptoms disappearing after a week to ten days.

No specific treatment was required, the patients being rested in bed until the cerebrospinal fluid returned nearly to normal. Some of the children showed hypochromic anaemia and were given oral iron therapy. Two children had mumps before the symptoms of meningitis appeared, and these were possibly of a different aetiology.

England and Wales in 1959

The number of deaths from cancer of the lung again increased in 1959. They numbered 21,063 (18,181 male and 2,882 female), an increase of 1,243 over the 1958 total. Deaths from coronary heart disease also increased. They numbered 84,920 in 1959 (52,192 male and 32,728 female), compared with 84,041 in 1958. The rate per thousand population increased from 1.86 to 1.87. The number of deaths from poliomyelitis was the lowest since separate records started in 1911; it was 66 (41 male and 25 female). Measles caused 98 deaths, whooping-cough 25, scarlet fever 1, and diphtheria 0. Deaths from motor accidents numbered 6,026, about 500 more than in 1958.—*Registrar-General's Quarterly Return*, No. 445, H.M.S.O.

Eire in First Quarter

The birth rate in Eire during the first quarter of 1960 was 20.5 per 1,000, the same as for the corresponding quarter in 1959. The number of births was 14,614. The number of deaths was 9,399, giving a rate of 13.2 per 1,000, being 1.5 below that of the first quarter of 1959. Deaths from tuberculosis numbered 135, being 123 of the respiratory system and 12 from other forms. Corresponding figures for the first quarter of 1959 were 157, 135, and 22 respectively.

There were 507 deaths of infants under 1 year, giving an infant mortality rate of 35 per 1,000 live births. In the corresponding quarter of 1959 it was 37. The maternal mortality rate was 0.4 per 1,000 registered births, compared with 0.6 in the 1959 first quarter.

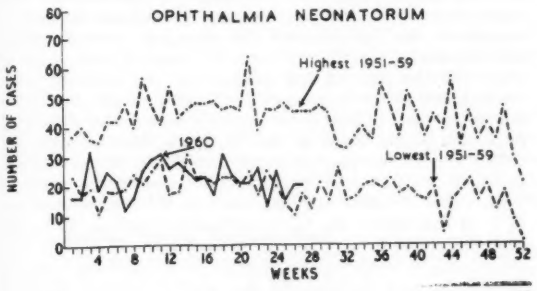
Infectious Diseases

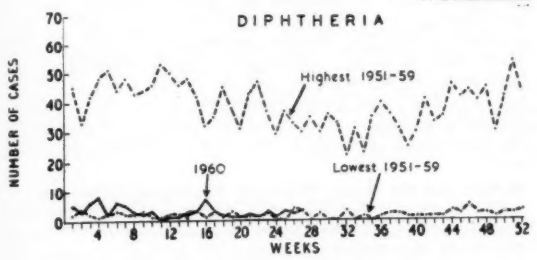
Areas where the numbers of notifications were high in the latest two weeks for which figures are available.

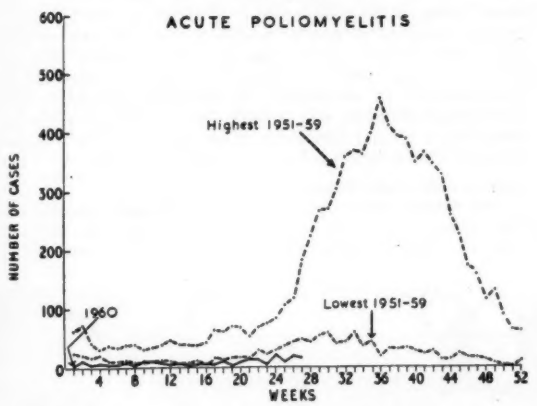
	Week Ending July 2	Week Ending July 9
Dysentery		
Cheshire	32	**35**
Birkenhead C.B.	14	**9**
Essex	43	**32**
Kent	10	**25**
Lancashire	146	**129**
Liverpool C.B.	20	**21**
Manchester C.B.	28	**21**
London	87	**63**
Islington	8	**12**
Middlesex	33	**26**
Surrey	9	**17**
Croydon C.B.	1	**13**
Yorkshire East Riding	7	**15**
Haltemprice U.D.	1	**10**
Yorkshire North Riding	12	**18**
Middlesbrough C.B.	9	**10**
Yorkshire West Riding	74	**75**
Leeds C.B.	28	**21**
Hemsworth R.D.	7	**23**
Glasgow	126	**76**
Diphtheria		
Warwickshire	1	**2**
Birmingham C.B.	1	**2**
Paratyphoid Fever		
Edinburgh	0	**3**

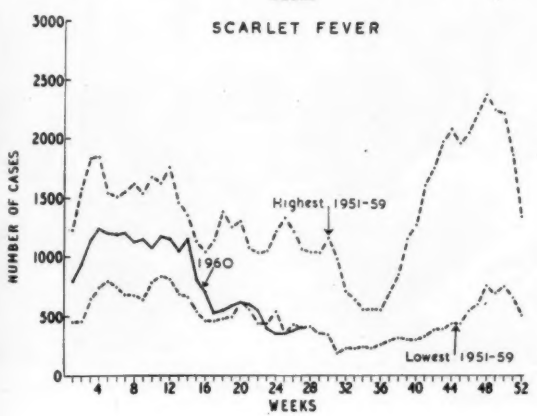
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1951–9 are shown thus ------, the figures for 1960 thus ———. Except for the curves showing notifications in 1960, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **July 2** (No. 26) and corresponding week 1959.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	2	0	2	0		20	18	4	0	
Dysentery ..	706	87	182	12	8	838	83	252	9	
Encephalitis, acute	3	0	0	0		4	0	0	0	
Enteric fever:										
Typhoid ..	2	0	1	0		4	0	0	1	
Paratyphoid ..	4	0	0	0		4	1	0	1	
Food-poisoning ..	241	34	61	0		222	35	6	0	
Infective enteritis or diarrhoea under 2 years				14	41				21	23
Measles*	2,674	134	40	5	15	10,116	342	216	339	130
Meningococcal infection	19	0	18	1		17	2	10	1	1
Ophthalmia neonatorum	20	1	7	0		10	0	3	0	1
Pneumonia† ..	145	7	118	5	4	180	8	130	3	
Poliomyelitis, acute:										
Paralytic ..	13	2	0	} 0	8	{ 31	15	2	} 1	
Non-paralytic ..	5	2	2			{ 22	2	1		
Puerperal fever§ ..	158	28	7	0	1	199	29	14	0	
Scarlet fever ..	378	14	24	10	13	902	59	72	26	15
Tuberculosis:										
Respiratory ..	397	36	61	19		497	53	65	21	
Non-respiratory	55	7	17	2		61	4	15	1	
Whooping-cough	1,776	132	158	3	15	699	32	72	26	63

DEATHS	1960					1959				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0		0		1	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	4	0	1	0	0	7	0	1	0	2
Influenza	3	0	0	0	0	3	1	0	1	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	1				0	0		
Pneumonia ..	322	23	10	10	8	299	28	10		7
Poliomyelitis, acute	1	0		0	0	2	1		0	0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	} 63	{ 8	2	0	0	} 62	{ 5	3	0	1
Non-respiratory		{ 0	0	0	1		{ 0	1	0	0
Whooping-cough	0	0	1	0	0	0	0	1	0	0
Deaths 0–1 year ..	267	29	26	8	19	211	21	22	8	17
Deaths (excluding stillbirths) ..	8,075	648	470	111	167	7,883	650	495	95	123
LIVE BIRTHS ..	15,470	1287	1012	267	402	14,860	1209	1012	286	424
STILLBIRTHS ..	302	24	23			276	22	30		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Director of N.I.M.R.

Professor P. B. MEDAWAR, D.Sc., F.R.S., has been named as Sir Charles Harington's successor as director of the National Institute for Medical Research, on the latter's retirement in August, 1962. Professor Medawar, who is 45, holds the Jodrell chair of zoology at University College London. He is an authority on immunology, and is particularly interested in the surgical problems of the transplantation of tissue.

New Chairman of Wellcome Trust

Sir HENRY DALE, O.M., F.R.S., the senior trustee of the Wellcome Trust, has served as chairman of the Trust for the last 22 years. Having now reached the age of 85 he has retired from the Trusteeship, but he has accepted the invitation of the Wellcome Trustees to retain his connexion with their activities in an advisory capacity. The Rt. Hon. Lord PIERCY, C.B.E., has succeeded him as chairman.

National Spastics Society

The National Spastics Society is putting its work on cerebral palsy at Guy's Hospital on a permanent footing by establishing there a research unit and a Research Professorship of Child Health. The unit—associated with 100 beds—will undertake research into the development of the normal child, and into factors from the earliest stages of pregnancy which may give rise to congenital defects. The Society has undertaken to provide £2m. over the next 10 years to establish the unit, the capital cost of which will be £450,000.

A Case of Mistaken Identity

In our issue of April 2, p. 1066, we printed a photograph, taken in 1860, of the dissecting-room at St. George's Hospital and in it identified an alert-looking young man, chin in hand, at the back of the room as Henry Gray. LEA AND FEBIGER, the Philadelphia publishers, quite rightly dispute this—on the authority of the anatomist's great-nephew, Mr. F. L. GRAY—saying that Gray is the dark figure in the left foreground by the cadaver's feet. Readers of the *Journal* may be interested to know how the mistake arose. The photograph we published, printed on the left below, was taken by Joseph Langhorn on March 27, 1860, and the St. George's Hospital Medical School authorities say that he must have taken two photographs on this occasion, for they hold an original print which is almost the same as the one published except that Gray has now retreated to the position at the back of the room picked out in our photograph of April 2. The only key to the photograph which St. George's possesses applies to this second version. The school says that until now nobody was aware that two photographs existed of this well-known group of Gray's students, and so, though the original print is very frail and has had to be photographed under glass, we reproduce it below.

Ministry of Health's 1959 Report

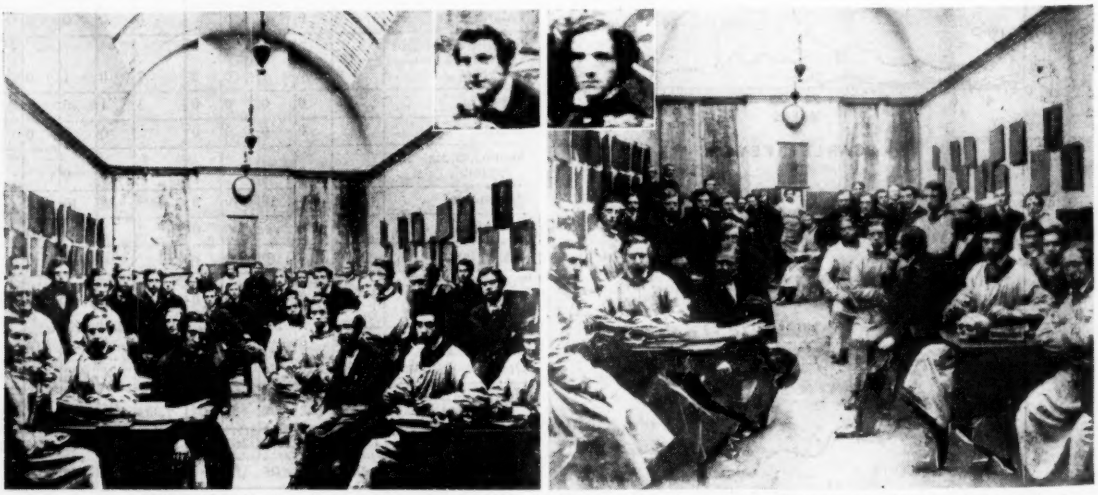
Expansion is seen as the keynote of the National Health Service's second decade—of which 1959 was the first year—with the end of "make do and mend" in the hospitals, the application of modern management techniques to various aspects of the Service, and the changing emphasis from institutional to community care, a change clearly seen in plans for the care of old people, for the mentally subnormal, and in the passing of the Mental Health Act, 1959, which, in the Minister of Health's view, was the most important single event in the National Health Service in 1959. Expansion was seen, too, in the cost of the services provided, which, at £671m., was £45m. up on the previous year. The Hospital and Specialist Services accounted for 57% of this figure, the General Medical Services 10%, the Pharmaceutical Service 10.25%—there were 214 million prescriptions, 16 million more than in 1958—and the General Dental Services 6.75%. So far as the hospital building programme is concerned, £31m. is likely to be spent in 1961 to 1962, a threefold increase on the period 1955 to 1956. More than 30 of the 180 major schemes approved at the beginning of 1960 were to cost more than £1m., eight new hospitals had been partly completed, nine begun, and 17 are being planned. (*Report of the Ministry of Health for the year ended 31st December, 1959*, H.M.S.O., price 13s. net.)

M.R.C. and Sir Henry Wellcome Travelling Fellowships

The Wellcome Trustees are providing £60,000 spread over five years to enable the Medical Research Council to award five Travelling Fellowships annually of approximately the same status as the Rockefeller Medical Fellowships and open to workers of similar academic seniority and distinction. The awards will be tenable in any country and for research in any field of medical science, but applications from workers in physiology, biochemistry, pharmacology, and tropical medicine may receive some preference, since the Trust has a special interest in these subjects. The Fellowships will be formally advertised later in the year.

Butterworth Gold Medal

The Butterworth Gold Medal is presented annually to the College of General Practitioners by Messrs. Butterworth and Co., the medical publishers, for an essay by a



Gray is wrongly identified in the photograph on the left: he is the figure by the cadaver's feet. In the right-hand picture he is at the back of the room.

member or associate of the College on a subject connected with general practice. The subject of this year's essay is "Television and Health." Essays, identified by motto only (with the author's name and address in a sealed envelope) and not exceeding 10,000 words, should be submitted to the chairman of the awards committee, The College of General Practitioners, 41, Cadogan Gardens, London, S.W.3, by September 17, 1960.

Buckston Browne Dinner

A Buckston Browne Dinner was held at the Royal College of Surgeons on July 13, when the principal guest was the AGA KHAN. The toast of "The College" was proposed by Mr. JULIAN AMERY, Parliamentary Under-Secretary of State for the Colonies. In responding, Sir JAMES PATERSON ROSS, P.R.C.S., emphasized that Buckston Browne's main purpose in enabling these dinners to be held was to encourage good fellowship between the Fellows and Members of the College. Equal numbers of Fellows and Members were invited to the dinners. The toast of the guests was proposed by Mr. A. DICKSON WRIGHT, and Mr. HAROLD CHRISTIE, Q.C., replied.

Dan Mason Nursing Research Fund

A survey which took in 200 hospitals in the United Kingdom and 2,000 nurses, of whom 1,000 were staff nurses, has recently been completed. Its findings on, among other subjects, the need for greater recognition of the status and responsibilities of staff nurses and the application of modern work-study methods to the work routine of wards and departments are fully discussed in *The Work, Responsibilities, and Status of the Staff Nurse* (The Dan Mason Nursing Research Committee of the National Florence Nightingale Memorial Committee of Great Britain and Northern Ireland, price 5s.).

King Edward's Hospital Fund for London

It was announced at the Fund's annual meeting on July 14 that the Fund has agreed, after discussions with the Ministry of Health, to embark in the autumn on a training programme for work-study officers. Income for the year amounted to £447,043, with legacies at £31,357, while expenditure amounted to £429,056. In its *Sixty-third Annual Report, 1959*, the Fund, discussing the principal need of the hospital world to-day, sees it as "constant vigilance lest complacency creeps in and the simpler and more elementary things are overlooked," such things as appetizing meals, quiet, and good human relationships.

Bowman Chair of Physiology, Birmingham University

Dr. I. E. BUSH, a member of the external staff of the Medical Research Council, has been appointed to the Bowman chair of physiology and to the directorship of the department of physiology at Birmingham University from October 1.

Dr. Bush, who was born in 1928, was educated at Bryanston School and at Pembroke College, Cambridge, and graduated with first-class honours in natural sciences at the University of Cambridge in 1949. From 1949 to 1952 he was a Medical Research Council Scholar—at the Physiological Laboratory until 1950 and at the National Institute for Medical Research from 1950 to 1952. In 1952 he was awarded a Commonwealth Fund Fellowship tenable successively at the University of Utah, U.S.A., and at the Massachusetts General Hospital. From 1953 to 1956 he was a part-time research assistant to the Medical Unit at St. Mary's Hospital, London, and, from 1956 to 1958, graduate assistant to the Regius professor of medicine at the University of Oxford. Dr. Bush is at present in charge of a group conducting research under Sir George Pickering, financed by the M.R.C. and the Rockefeller Foundation.

Birmingham University

Professor KENNETH MATHER, D.Sc., F.R.S., professor of genetics, Birmingham University, has been appointed vice-principal of the University for five years, from October 1, in succession to Professor G. W. H. LAMPE.

Mental Health Services

As was announced in Parliament last week (*Journal*, July 16, p. 240), the Mental Health Act, 1959, will come into full effect on November 1, but a number of sections—the most important relating to the local authority services—came into force on July 15. Circulars of guidance on these parts of the Act and on the regulations will be issued to local authorities, hospitals, and general practitioners during July and August. (A practitioners' guide to the Act was published in the *Journal*, December 26, 1959, pp. 1478–80.) The Mental Health (Powers of Inspection) Regulations, 1960, also comes into operation on July 15.

Royal Society of Medicine

At the annual meeting of Fellows held on July 5, with Sir GEOFFREY MARSHALL in the chair, the following officers were elected for the session 1960–1:

President, Lord ADRIAN, F.R.S.; *immediate past president*, Sir GEOFFREY MARSHALL; *honorary treasurers*, Dr. BASIL KIERNANDER, Air Vice-Marshal Sir AUBREY RUMBALL; *honorary secretaries*, Mr. TERENCE CAWTHORNE, Professor R. H. S. THOMPSON; *honorary librarians*, Sir JOHN RICHARDSON, Sir ERIC RICHES; *honorary editors*, Mr. SELWYN TAYLOR, Dr. R. I. S. BAYLISS, Dr. DAVID PYKE; *honorary directors of photography*, Mr. MYLES FORMBY, Dr F. C. KELLY.

"The Medical Directory 1961"

The annual schedule, upon the return of which the accuracy of *The Medical Directory* mainly depends, has recently been posted to all traceable members of the medical profession, and its speedy return would be appreciated. Any doctor who has not received the annual schedule, or who has mislaid it and would like a duplicate, is requested to communicate as soon as possible with the Editor, *The Medical Directory*, 104, Gloucester Place, London, W.1, including his full name and year of qualification for identification.

Anglo-American Medical Society

This Society has recently been founded in Cambridge and intends to meet every two months. Its aims are "to promote a close social and professional liaison between the American doctors in East Anglia and their British colleagues, and to examine more closely attitudes, values, and customs as they apply to medicine in both countries." Membership of the Society is open to medical practitioners of Britain and the U.S.A. Members may also be elected from closely allied professions at the discretion of the committee. Inquiries should be addresed to the Honorary Secretary, Mr. A. J. EDEN, Cedar Cottage, March Road, Wimblington, Cambridge.

Medical Fellows of the Royal Society

We regret the omission of the following name from the list published last week (p. 207):

1911

Professor W. H. LANG, Barker professor of cryptogamic botany, University of Manchester, noted for his work on living and fossil ferns and allied plants, and particularly distinguished for his investigations into the causes of the morphological differences between the sexual and asexual generations in the life cycle of ferns.

In Brief

A new medical centre has been planned for Melbourne University, costing over £A.2½m., and accommodating the departments of bacteriology, physiology, anatomy, and pathology, and a new medical library.

A plaque bearing the quotation *Hospes eram et collegistis me* (I was a stranger and you took me in) is being presented to Australia for erection in Canberra by the office of the U.N. High Commissioner for Refugees, Dr. A. R. LINDT. Australia has accepted 250,000 refugees since the second world war.

Safety belts for driver and front-seat passengers will in future be fitted as standard equipment in all Swedish Volvo 122 S saloon cars imported into Great Britain.

People in the News

Professor NAGUIB MAHFOUZ, emeritus professor of obstetrics, Cairo University, has been awarded the State Prize for 1960 and Gold Medal by the United Arab Republic for his services to the advancement of medical science.

Professor C. F. W. ILLINGWORTH, of Glasgow University, has been invited by the Royal College of Physicians and Surgeons of Canada to be the first McLauchlin Gallie visiting professor. The professorship has been financed by Mr. R. S. MCLAUCHLIN, a Toronto business man, in memory of the Canadian surgeon, the late Mr. W. E. GALLIE.

Dr. P. KORNER, who spent two years at the Postgraduate Medical School, London, has been appointed professor of physiology in the new medical school of the University of New South Wales.

Dr. A. G. EVERSON PEARSE has been made M.D. *honoris causa* of the University of Basle "for services to medical research and in the training of the rising generation."

COMING EVENTS

Royal College of Surgeons of England.—Special lecture: Dr. ZDENKO LOEWENTHAL (head of department of medical history, University of Belgrade), "The History of British-Jugoslav Medical Relations," July 27, 5 p.m., at the College, Lincoln's Inn Fields, London, W.C.2. Lecture open to those attending courses in the College and to medical practitioners, dental surgeons, and advanced students.

Anglo-American Medical Society.—First business meeting and discussion, September 7, "The Normal Pregnancy on Both Sides of the Atlantic." Honorary Secretary, Mr. A. J. EDEN, Cedar Cottage, March Road, Wimblington, Cambridge.

5th International Congress on Nutrition.—Washington, D.C., U.S.A., September 1–7. Sessions will include "The World's Increasing Population and Food Problems Resulting from It" and "The Prospect of Meeting Protein Needs." Details from the Secretariat, 9650, Wisconsin Avenue, Washington, 14, D.C., U.S.A.

"The Great Issues of Conscience in Modern Medicine."—Public convocation, Hanover, New Hampshire, U.S.A., September 8–10. Chairman, Dr. RENE DUBOS (member of the Rockefeller Institute, New York). Other participants will include MAHOMEDALI CURRIM CHAGLA (Indian Ambassador to the United States and Mexico), ALDOUS HUXLEY, Sir CHARLES SNOW, Sir GEORGE PICKERING, Dr. WARREN WEAVER, Dr. GEORGE KISTIAKOWSKY, Dr. WALSH MCDERMOTT, Dr. BROCK CHISHOLM, Dr. RALPH GERARD, Dr. WILDER PENFIELD, and Dr. SANDOR RADO.

14th General Assembly, World Medical Association.—Berlin, September 16–22. Details from Bundesärztekammer-Kongressbüro, 1, Haedenkampstrasse, Köln-Lindenthal, Germany.

University of Glasgow and R.F.P.S.—"Current Trends in Surgery," September 26 to October 8. For details see advertisement p. 52.

NEW ISSUES

BRITISH JOURNAL OF OPHTHALMOLOGY

Investigation of the Sources of Trachoma in the White School Population of Western Australia. I. Mann.
Experimental Treatment of Australian Trachoma with Special Reference to Lederkyn. I. Mann.
A Second Survey with Electro-oculography. B. Shackel and J. R. Davis.
Gonio-Vessels in Normal and Abnormal Eyes. S. Chatterjee.
Severe Ophthalmological Complications Following Favism. C. Choremis, T. Joannides, and B. Kyriakides.
Surgical Results in Acute Glaucoma. P. A. Graham and P. R. Stevens.
Metabolism of the Developing Retina. III. C. Graymore.
New Technique for Opening the Canal of Schlemm. Redmond Smith.
Photography of Lens Opacities by Trans-Scleral Illumination. A. J. Ogg.
Choroidal Melanoma Invading the Orbit without Distant Metastases. V. H. Smith and A. Nicol.
Value of Gluck's Metallic Post-operative Eye Shield. A Arruga.
Correspondence.
Reviews.

Volume 44, No. 6. (Monthly; £6 annually. With *Ophthalmic Literature* and Index, £9.)

BRITISH JOURNAL OF VENEREAL DISEASES

The Treponematoses as a World Problem. T. Guthe.
The Evolutionary Cycle of the Treponematoses. R. R. Willcox.
Syphilis in Tunisia. Ladjimi.
Treponematosis in Singapore. L. M. Ram.
Prophylaxis against the Venereal Diseases. C. Ducrey.
Venereal Disease in the Female. M. Cardia and A. da Fonseca.
Group Discussion with Male V.D. Patients. C. S. Nicol, A. J. Dalzell-Ward, and M. C. Haworth.
The Clients of Prostitutes. T. C. N. Gibbens and M. Silberman.
Psychological Pattern of Patients with Non-gonococcal Urethritis. A. Siboulet.
The Road to Promiscuity. J. O'Hare.
Venereal Diseases in Bulgaria. P. Popchristov.
Problems of the V.D. Campaign in Czechoslovakia. E. Heygi.
Incidence of Venereal Disease in Italy. V. Coffari.
The Realities of the Campaign against Venereal Disease. A. da Fonseca.
Epidemiology of Venereal Disease in Portugal during the Second World War. F. N. Brandaõ.
Campaign against V.D. in Mexico. R. Bustillos Mendez.
The Campaign against Syphilis in Hungary. F. Földvari and St. Károlyi.
Reviews.
Obituary.
Abstracts.

Volume 36, No. 2. (Quarterly; £3 annually.)

THORAX

Coronary Arteriography. Kingsley Lawrance.
The Radiological Diagnosis of Asbestosis. Roger Williams and P. Hugh-Jones.
The Significance of Lung Function Changes in Asbestosis. Roger Williams and P. Hugh-Jones.
Malignant Teratoid Tumour of the Lung: Malignant Hamartoma. Torben Schiødt and Kaj Gotlieb Jensen.
The Effect of Intermittent Positive Pressure Breathing on the Lung Compliance and Intrapulmonary Mixing of Gases. Peter A. Emerson, G. E. Torres, and Harold A. Lyons.
Measurement of the Bronchial Mucous Gland Layer: A Diagnostic Yardstick in Chronic Bronchitis. Lynne Reid.
Bronchial Biopsy in Chronic Bronchitis and Asthma. A. A. Glynn and L. Michaels.
Detection of Bronchial and Arterial Obstruction by Continuous Gas Analysis from Individual Lobes and Segments of the Lung. P. Hugh-Jones and J. B. West.
Cavo-pulmonary Anastomosis. B. J. Bickford and F. Ronald Edwards.
Absence of Mesothelial Cells from Tuberculous Pleural Effusions. A. I. Spriggs and M. M. Boddington.
A Case of Bilateral Superior Venae Cavae with a Closed Coronary Sinus. W. G. Harris.
Supernumerary Tracheal Bronchus. A. M. B. Golding.
The Use of the P Wave for Control of a Pacemaker in Heart Block. C. K. Battye and F. E. Weale.
A Disposable Rotating Oxygenator Capable of Being Sterilized by Heat for a Heart-Lung Machine. Michael Wilson and Keith Vowles.

Volume 15, No. 2. (Quarterly; £3 annually.)

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Wednesday, July 27

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Dr. T. B. Quigley (Harvard): Ligament Rupture at the Ankle and Knee; Lessons Learned from the Playing Field.
ROYAL FREE HOSPITAL, Gray's Inn Road, London, W.C.—5.15 p.m., Dr. William B. Bean (Iowa City): Rare Diseases: Chronic Atrophic Polychondritis.
SOCIETY FOR ENDOCRINOLOGY:—At Royal Society of Tropical Medicine and Hygiene, 5.15 p.m., Professor B. A. Houssay (Buenos Aires): An Argentine Trail in Hypophyseal Research.

Thursday, July 28

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Cecil Joll Lecture by Professor E. E. Dunlop: Carcinoma of the Oesophagus.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Ancill.—On July 12, 1960, at Wells and District Hospital, Wells, Somerset, to Sheilah Kendrick, wife of Dr. R. J. Ancill, a son—Aidan Kendrick.
Briffa.—On July 9, 1960, at the Hospital of St. John and St. Elizabeth, London, N.W., to Dorothy (formerly Burgess), M.D., wife of J. V. Briffa, M.D., L.M., a daughter.
Gordon-Russell.—On July 12, 1960, at Devizes Maternity Hospital, to Peggy and James Gordon-Russell, a sister for Martin and Fiona—Elspeth.
Michell.—On July 14, 1960, at the Middlesex Hospital, London, W., to Anne (formerly Pearce), wife of Dr. Guy Michell, a brother for Christopher and Elizabeth—Jonathan.
Wooller.—On July 3, 1960, at H. M. Stanley Hospital, St. Asaph, Flints., to Deborah (formerly Hardman), wife of Dr. H. O. Wooller, a son—Timothy Owen.

DEATHS

Browne.—On June 13, 1960, Dominick Joseph Browne, L.R.C.P.&S.I., of 51, Frankley Beeches Road, Northfield, Birmingham.
Inkster.—On June 15, 1960, John Inkster, M.D., F.R.C.P., D.P.H., formerly of Middlesbrough, Yorkshire, aged 72.
Marshall.—On June 15, 1960, George Guthrie Marshall, M.B., Ch.B., D.P.H., D.A., of 224, Abbeydale Road South, Dore, Sheffield, Yorks.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

"Mucous Colitis"

Q.—*What is the treatment of mucous colitis with severe abdominal discomfort and diarrhoea? Alimentary neoplasm has been excluded.*

A.—The term mucous colitis is a confusing one, suggesting an inflammatory lesion when, in fact, none is present, and the term irritable colon syndrome is to be preferred. Treatment consists in psychological reassurance and rehabilitation, dietary care, and the use of antispasmodics and sedatives.

It is first necessary to be in a position to reassure the patient that no serious organic disease is present and that the condition is more benign than colitis, diverticulitis, or neoplasm, and to this end a recent barium enema and sigmoidoscopy should have been performed. Most patients with mucous colitis are tense, nervous individuals and the condition is often a symptom of conflict or stress induced by financial, sexual, or environmental factors which may be resolved by sympathetic discussions, formal psychotherapy being rarely necessary.

In bouts of diarrhoea a low-residue diet is prescribed, avoiding fruit and vegetables. Foods rich in carbohydrates or cellulose, which tend to cause excessive flatus, and the intake of coffee and alcohol should be restricted. It is often the case that the diarrhoea is a spurious one alternating with constipation, when small hard stools are passed. Here cooked fruit, vegetables, and cereals should be added to promote more soft stools. A bulk-forming laxative is often necessary, but irritant laxatives should be avoided.

Antispasmodics are the most valuable drugs in the treatment of this condition. Tincture of belladonna 15 drops or atropine 0.3–0.6 mg. orally three to four times daily are useful, but better results are obtained by proprietary "spansule" preparations containing powdered belladonna, when an 8–12-hour action is obtained. There is little evidence that the newer anticholinergic drugs, such as propantheline bromide, tricyclamol, or "buscopan" in comparable dosage have any better effect, but these may be tried if atropine fails or induces too many side-effects.

Sedatives such as phenobarbitone, amytal, or meprobamate are extremely helpful in the anxious patient, and several proprietary combinations of sedatives and antispasmodics are available. Opiates should be avoided, since they tend if anything to increase intestinal spasm.

Vitamins for the Aged

Q.—*Are vitamin D and pyridoxine necessary in a multiple-vitamin preparation for the aged? Can vitamin D, 500 units daily in a multiple preparation, have any harmful effects if administered to patients over 60 for an indefinite period?*

A.—There is no evidence that adults need any dietary supply of either vitamin D or pyridoxine.[1] Vitamin D is formed in adequate amounts in the skin. It is possible that old people who spend their lives indoors may become deficient in this vitamin, but there is no proof that this happens. Attempts to induce pyridoxine deficiency experimentally in adults have failed to produce symptoms; and assertions that pyridoxine is beneficial in certain cardiovascular and nervous disorders have no firm foundation. Pyridoxine is abundant in many foods, being supplied in crude sources of vitamin-B complex. The giving of 500 units of calciferol daily to an elderly patient for an indefinite period would probably be entirely safe.

REFERENCE

[1] Davidson, L. S. P., Meiklejohn, A. P., and Passmore, R. A., *Human Nutrition and Dietetics*, 1959. E. and S. Livingstone, Edinburgh.

Writer's Cramp

Q.—*What is the cause of writer's cramp? Can it be cured?*

A.—Writer's cramp is due to spasm of the various muscles concerned in the act of writing, which becomes progressively more difficult to perform. It may be associated with pain and tremor in the affected hand. There are no abnormal neurological signs, and in the early stages other fine movements involving the same muscles are unaffected. It is thought to be an occupational neurosis, and often other hysterical manifestations are present. The patient's job usually entails writing with speed and accuracy for long periods, and similar occupational neurosis has also been described in telegraphists and pianists.

Care must be taken to exclude organic lesions of the central nervous system, in which there is loss of the ability to perform fine movements, although here the loss is not confined to one movement. It is difficult to cure and the patient may have to seek alternative employment. In any event an adequate period of rest from writing is advisable and an attempt should be made to discover any precipitating psychiatric factors which might be amenable to adjustment. Instruction in muscular relaxation and re-educational exercises may be of value.

Salt in Cheese

Q.—*Which of the ordinary cheeses contain the least salt?*

A.—The cheeses lowest in salt, so far as can be judged from their sodium contents, are cream cheese, with 250 mg. of sodium per 100 g., and cottage cheese, with 290 mg. Most ordinary full-fat cheeses contain about 700 mg. of sodium per 100 g., and in processed cheeses sodium may reach 1,500 mg. In cream cheese the low sodium content is associated with high contents of water and fat, and in cottage cheese with a high content of water but low fat. Cream cheese has the lowest ratio between sodium and calories, and cottage cheese the lowest ratio between sodium and protein.

Immunizations and Eczema

Q.—*Are there any special hazards attached to vaccinating and immunizing a child suffering from infantile eczema?*

A.—A child with infantile eczema should not be vaccinated unless the reasons are compelling. The risk is of the supervention of virus infection on the eczema if it is active. This may spread widely over the skin and be accompanied by systemic infection which may be fatal. Apart from this, vaccination is likely to aggravate the eczema. Other immunizing injections, as for whooping-cough, diphtheria, and poliomyelitis, may also aggravate eczema temporarily, but this should not prevent their proper use if the eczema is not active and severe.

Toxicity of Saccharin

Q.—*Is there any evidence to suggest that saccharin is cardiotoxic?*

A.—Saccharin is a white crystalline substance which is the anhydride of *O*-sulphamidobenzoic acid. It is about 400 times as sweet as sugar but has no food value. In pharmacological tests it has been found to be non-toxic even in doses much larger than those in which it is normally used for sweetening foods or beverages. Almost the whole amount administered is excreted in the stools and urine within 24 hours.

Loss of Weight After Confinement

Q.—*Is there any satisfactory treatment for loss of weight, particularly in the breasts, after confinement?*

A.—General loss of weight following pregnancy deserves the fullest investigation to exclude a causal organic disease. If none is found the logical treatment is to increase the food intake of the patient. An anabolic agent such as

norethandrolone might also be helpful. If the adipose tissue can be increased this may improve the shape of flaccid breasts. Physiotherapy involving pectoral muscle exercises is sometimes advised, but the results are not convincing. If the breasts are pendulous rather than small, plastic surgery has something to offer but would be best deferred until child-bearing is completed.

Antimalarial Drugs in Rheumatoid Arthritis

Q.—*Is there any evidence that hydroxychloroquine is better than chloroquine in the treatment of rheumatoid arthritis?*

A.—The evaluation of new drugs in the treatment of rheumatoid arthritis is notoriously difficult, because of the variation in severity and activity that is part of the natural history of the disease and the lack of precise parameters of assessment. The effectiveness of the antimalarial drugs is still not certain, but reports that they exert a significant effect are appearing in increasing numbers.

Retinopathy, which may lead to blindness, has been reported after the prolonged use of chloroquine,[1 2] and less serious, although troublesome, side-effects are nausea, bleaching of the hair, and corneal opacities. Hydroxychloroquine is less toxic dose for dose than chloroquine, but there is no evidence that it is more effective.

The eventual role these drugs will play in the management of rheumatoid arthritis has yet to be worked out, but they are not a substitute for adequate salicylate therapy, nor, in the case of overwhelming disease, for systemic steroid.

REFERENCES
[1] Hobbs, H. E., Sorsby, A., and Freedman, A., *Lancet*, 1959, **2**, 478.
[2] Fuld, H., ibid., 1959, **2**, 617.

Sterilizing Crockery in Sanatoria

Q.—*What is the best method of sterilizing patients' dishes and cutlery in a sanatorium where the buildings are at some distance from each other?*

A.—Undoubtedly the best method of sterilizing patients' crockery and cutlery in a sanatorium is by boiling. Each washing-up unit should be equipped with a sterilizer. It is probable that efficient washing-up, with a final rinse under running hot water, and rack drying will remove all traces of infection. The writer believes that tuberculosis is rarely if ever spread by crockery or cutlery, but when there is any risk of infection small children should be provided with their own utensils, which must be washed up separately. For maximum safety in hospital, sterilization by boiling is advisable.

Recurrent Bartholinitis

Q.—*What is the treatment for recurrent attacks for over a year of bartholinitis with abscess formation in a woman aged 45? Only one side is affected. Penicillin now has little effect.*

A.—Recurrent abscess formation usually means an underlying persistent chronic inflammatory lesion in Bartholin's gland or duct. This may be made manifest by finding a small cyst or a firm nodular enlargement of the gland after the acute inflammatory process has subsided. Such a lesion should be excised during a period of quiescence.

If the gland and duct are not palpable between attacks then excision is impracticable and active treatment should await the next abscess formation. Meanwhile, however, any source of chronic infection in the cervix or vagina should be eliminated. Antibiotics should not be given if another acute attack occurs, and when the abscess is pointing it should be opened by an adequate surgical incision rather than be allowed to burst spontaneously. A thorough opening of all compartments of the abscess may alone ensure a permanent cure. It may be added that some surgeons, at the time of the incision, now aim to marsupialize the abscess or cyst cavity to leave a permanent sinus which provides effective drainage of the gland products in the future.

NOTES AND COMMENTS

Sensitivity to Sulphonamides.—Dr. R. G. PARK (Wellington, New Zealand) writes: I cannot let go unchallenged a statement ("Any Questions?" March 19, p. 892) in answer to a question on sensitivity to sulphonamides. Your reply states: "Effective desensitization procedures are unknown." On the contrary, desensitization to sulphonamides is uniformly successful. I reported briefly on this question in 1944[1 2] and it was discussed more fully by Tate and Klorfajn in the same year.[3] In these days of alternative antibacterial substances it is not often necessary to carry out this procedure, but it can be done just as effectively as has been achieved with penicillin and streptomycin.

REFERENCES
[1] Park, R. G., *Lancet*, 1944, **1**, 401.
[2] —— *Brit. med. J.*, 1944, **2**, 816.
[3] Tate, B. C., and Klorfajn, I., *Lancet*, 1944, **1**, 39.

OUR EXPERT replies: In 1944 Tate and Klorfajn concluded that "desitization had been achieved, but whether this will be permanent or the method universally applicable is not yet known." In 1944 Dr. Park published two case reports of successful desensitization to sulphonamides in one of which, seen twelve months later, the sensitivity had only partially returned. Goodman and Gilman[1] write: "Readministration of a sulphonamide to a patient who has previously experienced rash or fever from drugs of this class may result in a recurrence of the eruption or in a more serious reaction such as nephrosis and acute toxic hepatitis. Sensitization to sulphonamides may last for several years, since effective desensitization procedures are unknown." I would emphasize the word "effective" and agree with the views of Goodman and Gilman.

REFERENCE
[1] Goodman, L. S., and Gilman, A., *The Pharmacological Basis of Therapeutics*, 1955, 2nd ed., p. 1298. Macmillan, New York.

Haemophilia in Jews.—Dr. F. NOUR-ELDIN (Brentwood, Essex) writes: In respect of the query raised in your answer ("Any Questions?" June 4, p. 1752) regarding information by other workers, I would like to mention that I have already collected special data related to the above. The two following observations gave me the impression that the percentage of Jews in patients with Christmas disease is higher than that in cases of haemophilia. (1) In a series of 222 patients with haemophilia and 40 cases of Christmas disease I have found bleeding after circumcision to be recorded in 14 patients (6.3%) with haemophilia and six cases (15%) of Christmas disease. (2) Religions registered on in-patient records showed predominance of the Jewish faith among patients with Christmas disease. Accordingly I carried out a further study regarding this point on unselected cases comprising 130 haemophilic patients and 25 cases of Christmas disease. Eight of the former group and five of the latter were Jews. It would be of particular interest if other centres where these patients attend would verify my observations by collecting specific data.

Correction.—In Professor Ingram's review of *Progress in the Biological Sciences in Relation to Dermatology*, edited by Arthur Rook (July 9, p. 119) he mentioned that 17 papers were included. This should have been 37.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Refresher Course for General Practitioners, Volume 3 (26s. 9d.).

Clinical Pathology in General Practice (22s. 3d.).

Any Questions?, Volume 3 (8s. 3d.).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. Authors overseas should indicate on MSS. if reprints are required, as proofs are not sent abroad.

ADVERTISEMENTS should be addressed to the Advertisement Director, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: *Britmedads, Westcent, London.*

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 4499. TELEGRAMS: *Medisecra, Westcent, London.*

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.